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Medical Guidelines

Rheumatoid Arthritis

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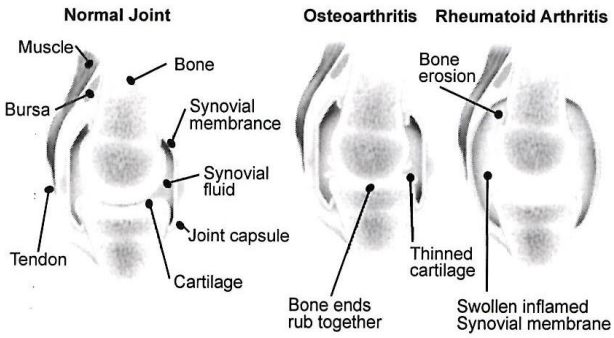
Introduction:

Rheumatoid arthritis Rheumatoid arthritis (RA) is the most common cause of inflammatory joint disease. It commonly affects younger women aged 20 to 50 years. The diagnosis of RA is not always easy to make. However, if a patient is suspected to have the condition he or she should, in most cases, be considered for treatment to slow down the progression of the disease. This often requires an urgent referral to a rheumatologist. Unfortunately, rheumatology waiting times are notoriously long. There are only 25 qualified Rheumatologists in Pakistan Here comes the need to train G.Ps in diagnosing RA at an early stage. This should reduce the morbidity associated with this potentially disabling disease.

What is rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic, systematic inflammatory disorder that may affectt many tissues and organs, but principally attacks synovial joints. The process produces an inflammatory response to the synovium (synovitus) leading to the destruction of the articular cartilage and ankylosis of the joints. Rheumatoid arthritis can also produce diffuse inflammation in the lungs, and pericardium. pleura and sclera, and also nodular lesions, most common in subcutaneous tissue under the skin. Although the cause of rheumatoid arthritis is unknown, autoimmunity plays a pivotal role in its chronicity and progression.



Normal and Arthritic Joints

Typical Presentation

Patients commonly present with pain and stiffness in multiple joints, although one one-third of patients initially experience symptoms at just one location or a few

scattered sites. In most patients, symptoms emerge over weeks to months, starting with one joint and often accompanied by prodromal symptoms of anorexia, weakness, or fatigue. In approximately 15 percent of patients, onset occurs more rapidly over days to weeks.

Joints Involvement

RA usually affects joints symmetrically Joints most commonly affected are those with the highest ratio of synovium to articular cartilage. The wrists are nearly always involved, as are the proximal interphalangeal and metatarsophalangeal joints. Other frequently affected joints are elbows, should er, knee and ,ankle joints.

Rheumatoid joints typically are boggy, tender to the touch, and warm, but they usually are not erythematous. Some patients complain of "puffy" hands secondary to increased blood flow to inflamed areas. Muscles near inflamed joints often atrophy.. Morning stiffness lasting at least 45 minutes after initiating movement is common. Patients often hold joints in flexion to minimize painful distension of joint capsules. Low-grade fever, fatigue, malaise, and other systemic complaints may arise, especially in an acute presentation. As the pathology progresses the inflammatory activity leads to tendon tethering and erosion and destruction of the joint surface, which impairs range of movement and leads to deformity.

Hands affected by RA

Rheumatoid Nodule

The rheumatoid nodule, which is often subcutaneous, is the feature most characteristic of rheumatoid arthritis. The typical rheumatoid nodule may be a few millimetres to a few centimetres in diameter and is usually found over bony prominences, such as the olecranon, the calcaneal tuberosity, the metacarpophalangeal joint, or other areas that sustain repeated mechanical stress. Nodules are associated with a positive RF (rheumatoid factor) titer and severe erosive arthritis..

Constitutional symptoms

Constitutional symptoms including fatigue, low grade fever, malaise, morning stiffness, loss of appetite and loss of weight are common systemic manifestations seen in patients with active rheumatoid arthritis

Other Manifestations.

Fibrosis of the lungs and Pleural effusions are also associated with rheumatoid arthritis

The eye is directly affected in the form of episcleritis and keratoconjunctivitissicca, which is a dryness of eyes and mouth caused by lymphocyte infiltration of lachrimal and salivary glands. Hepatic involvement in

RA is essentially asymptomatic. Anemia, Carpal Tunnel Syndrome and also occur.

DIAGNOSTIC TESTS

Rheumatoid arthritis is primarily a clinical diagnosis. No single diagnostic test definitively confirms the diagnosis of rheumatoid arthritis. The American College of Rheumatology recommends that baseline laboratory evaluations include a complete blood cell count with differential,

rheumatoid factor, and erythrocyte sedimentation rate (ESR) or Creative protein (CRP). Baseline evaluation of renal and hepatic function also is recommended because these findings will guide medication choices.

Laboratory tes	Associated findings
Creative protein	Typically increased to>0.7 picograms per mL; may be used to monitor disease course.
Erythrocyte sedimentation rate	Often increased to>30 mm per hour; may be used to monitor disease course.
Hemoglobin/hematocrit	Slightly decreased; hemoglobin averages around 10 g per dL. (100 g per L); normochromic anemia, also may be normocytic or microcytic
Liver function	Normal or slightly elevated alkaline phosphatase
Platelet	Usually increased
Radiographic findings of involved joints	May be normal or show osteopenia or erosions near joint spaces in early disease; wrist and ankle films are useful as baselines for comparison with future studies.
Rheumatoid factor	Negative in 30 percent of patients early in illness; if initially negative, can repeat six to 12 months after disease onset; can be positive in numerous other processes (e.g., lupus; scleroderma; Sjögren's syndrome; neoplastic disease; sarcoidosis; various viral, parasitic, or bacterial infections); not an accurate measure of disease progression.
White blood co	May be increased
Anticycliccitrullinated peptide antibody	Tends to correlate well with disease progression; increases sensitivity when used in combination with rheumatoid factor, more specific than rheumatoid factor (90 versus 80 percent); not readily available in many laboratories.
Antinuclear antibody	Limited value as a screening study for rheumatoid arthritis
Complement levels	Normal or elevated
Immunoglobulins	Elevated alpha-1 and alpha-2 globulins possible
Joint fluid evaluation	Consider if an affected joint can be tapped and diagnosis is uncertain; straw colored fluid with fibrin flecks often seen; fluid may clot at room temperature; 5,000 to 25,000 white blood cells per mm (5 to 25 x 10 per L) with 85 percent polymorphonuclear leukocytes a common finding: in rheumatoid arthritis, cultures are negative, there are no crystals, and fluid glucose level typically is low.
Urinalysis	Microscopic hematuria or proteinuria may be present in many connective tissue diseases.

X-ray of the hand in rheumatoid arthritis

X-rays of the hands and feet are generally performed in people with a polyarthritis. In rheumatoid arthritis, there may be no changes in the early stages of the disease, or the x-ray may demonstrate juxta-articular osteopenia, soft tissue swelling and loss of joint space. As the disease advances, there may be bony erosions and sublaxation. X-rays of other joints may be taken if symptoms of pain or swelling occur in those joints. Other medical imaging techniques such as magnetic resonance imaging and ultrasound are also used in rheumatoid arthritis.

Diagnostic criteria

The American College of Rheumatology has defined (1987) the following criteria for the classification of rheumatoid arthritis Morning stiffness of>1 hour most mornings for at least 6 weeks.

- Arthritis and soft-tissue swelling of>3 of 14 joints/joint groups, present for at least 6 weeks
- Arthritis of hand joints, present for at least 6 weeks Symmetric arthritis, present for at least 6 weeks
- Subcutaneous nodules in specific places
- Rheumatoid factor at a level above the 95th percentile
- Radiological changes suggestive of joint erosion
- At least four criteria have to be met for classification as RA

Management

Joint destruction in rheumatoid arthritis begins within a few weeks of symptom onset; early treatment decreases the rate of disease progression. Therefore, it is imperative to diagnose the disease and initiate treatment as soon as possible. The optimal treatment of RA requires a comprehensive program that combines medical, social, and emotional support for the patient. It is essential that the patient and the patient's family be educated about the nature and course of the disease.

Goal of treatment

Reducing pain and discomfort Preventing deformities and loss of joint function Maintaining a productive and active life.

Treatment options

Pharmacological Treatment Reduction of joint stress Physical and occupational therapy Surgical intervention

Non-steroidal Anti-inflammatory Agents (NSAIDs)

The major effect of these agents is to reduce acute inflammation there by decreasing pain and improving function. These drugs alone do not change the course of the disease of rheumatoid arthritis or prevent joint destruction.

There are a large number of NSAIDs and at full dosages all are potentially equally effective. However, there is a great deal of variation in tolerance and response to a

particular NSAID, Many different NSAIDS are available, including ibuprofen naproxen meloxicam, diclofenac

indomethicin, piroxicam and COX-2 inhibitors. Longer acting NSAIDs that allow daily or twice daily dosing may improve compliance A higher dose is often required to decrease inflammation. A lower dosage can initially be used if the patient is elderly or if the patient suffers from conditions that increase the risk for toxicity. If a particular preparation is ineffective after a 4-week trial or is not tolerated, then another NSAID can be initiated. No one NSAID has been demonstrated to be better than another for the treatment of rheumatoid arthritis nor have the COX-2 agents been shown to be superior to traditional NSAIDS in terms of effectiveness

Corticosteroids

Corticosteroids have both anti-inflammatory and immunoregulatory activity. They can be given orally, intravenously, intramuscularly or can be injected directly into the joint. Corticosteroids are useful in early disease as temporary adjunctive therapy while waiting for DMARDs to exert their antiinflammatoryeffects, Corticosteroids are also useful as chronic adjunctive therapy in patients with severe disease that is not well controlled on NSAIDs and DMARDs. They can also be used in flare ups. The usual dose of prednisone is 5 to 10mg daily

Recent studies suggest that low dose prednisone may have effects as a "disease modifying agent in RA, especially when used in combination with other DMARD medications.

Repetitive short courses of high-dose corticosteroids, intermittent intramuscular injections, adrerticotropic hormone injections, and the use of corticosteroids as the sole therapeutic agent are all to be avoided.

Intra-articular corticosteroids are effective for controlling a local flare in a joint without changing the overall drug regimen.

Disease Modifying Anti-rheumatic Drugs (DMARDS)

DMARD agents have been shown to alter the disease course and improve radiographic outcomes. DMARDs have an effect upon rheumatoid arthritis that is different and may be more delayed in onset than either NSAIDs or corticosteroids. In most cases, when the diagnosis of rheumatoid arthritis is confirmed, DMARD agents should be started. The presence of erosions or joint space narrowing on x-rays of the involved joints is a clear indication for DMARD therapy, however one should not wait for x-ray changes to occur. The currently available drugs include:

- Methotrexate
- Hydroxychloroquine
- Sulfasalazios
- Leflunomide
- Tumor Necrosis Factor Inhibitors--etanercept and infliximab
- T-cell Costimulatory Blocking Agents-abatacept B cell Depleting Agents-rituximab Interleukin-1 (IL-1) Receptor Antagonist Therapy-anakinra
- Intramuscular Gold

- Other Immunomodulatory and Cytotoxic agents-azathioprine cyclophosphamide, and cyclosporine A

We will discuss only 3 most commonly used DMARDS

Methotrexate

Methotrexate is now considered the first-line DMARD agent for most patients with RA. It has a relatively rapid onset of action at therapeutic doses (6-8 weeks), good efficacy, favorable toxicity profile, ease of administration, and relatively low cost. The majority of patients continue to take-Methotrexate after 5-years, fur more than other therapies reflecting both its efficacy-and-tolerability. Methotrexate is effective in reducing the signs and symptoms of RA, as well as slowing or halting radiographic damage, it was as effective as leflunomide and sulfasalazine in one study, and its effectiveness given early and in higher doses approached the efficacy of etanercept and adalimumab as single therapies in terms of signs and symptom improvement.

Dosage:

Methotrexate can be started at a dose of 10 mg per week, and increased to 20 mg per week by week 8. Maximal dose is usually 25 mg per week but is sometimes increased further Methotrexate is usually given orally but can be given by subcutaneous injection. Patients starting methotrexate should be carefully evaluated for renal insufficiency, acute or chronic liver disease, significant alcohol intake or alcohol abuse, leukopenia and thrombocytopenia. Concomitant use of methotrexate and trimethoprim is to be avoided. The coadministration of NSAIDS with methotrexate is routine in patients with rheumatoid arthritis and is considered safe by rheumatologists as long as liver function tests are closely monitored.

Hydroxychloroquine

Hydroxychloroquine is an antimalarial drug which is relatively safe and well-tolerated agent for the treatment of rheumatoid arthritis. Because these drugs have limited ability to prevent joint damage on their own, their use should probably be limited to patients with very mild and nonerosive disease: Hydroxychloroquine is sometimes combined with methotrexate for additive benefits for signs and symptoms or as part of a regimen of triple therapy" with methotrexate and sulfasalazine

Dosage: The usual dose is 400mg/day but 600mg/day is sometimes used. It may be prescribed as a single daily dose or in divided doses twice per day. Usual Time to Effect Is 2 to 4 months. Most agree that if a patient shows no response after 5-6 months that this should be considered a drug failure.

Sulfasalazine

Sulfasalazine is an effective DMARD for the treatment of RA. Its effectiveness overall is somewhat less than that methotrexate, but it has been shown to reduce signs and symptoms and stow radiographic damage. It is also given in conjunction with methotrexate and hydroxychloroquine as part of a regimen of "triple therapy" which has been shown to provide benefits to patients who have had inadequate responses to methotrexate alone..

Dosage:

The usual dose is 2-3 grams per day in a twice daily dosing regimen. The dose may be initiated at gram per day and increased as tolerated. Usual Time to Effect is 6 weeks to 3 months.

Reduction of joint stress

Because obesity stresses the musculoskeletal system, ideal body weight should be achieved and maintained, Rest, in general, is an important feature of management. When the joints are actively inflamed, vigorous activity should be avoided because of the danger of intensifying joint inflammation or causing traumatic injury to structures weakened by inflammation. On the other hand, patients should be urged to maintain a modest level of activity to prevent joint laxity and muscular atrophy, Splinting of acutely inflamed joints, particularly at night and the use of walking aids (canes, walkers) are all effective means of reducing stress on specific joints. A consultation with a physical and an occupational therapist is recommended early in the course

Monitoring of Rheumatoid Arthritis

If patient is on Methotrexate, monitor CBC, SGPT and serum Creatinine every 6-8 weeks, when stable maximum interval should be 12 weeks If patient is on Hydroxychloroquin get eye examination done at beginning and every 6 months.DAS28 disease activity score Rheumatologists use DAS28 disease activity score on a scale from 0 to 10 to assess current activity of the rheumatoid arthritis.

1. The number of swollen joints using 28-joint counts

2. The number of tender joints using 28-joint counts

3. The ESR/CRP should be measured

4. The patients general health activity measured on a Visual Analogue Scale (VAS) of 100 mm ie the patient is asked about the improvement he feels on a scale from 0-100

This information is calculated By using DAS28 calculator

A DAS28 above 5.1 means high disease activity whereas a DAS28 below 3.2 indicates low disease activity. Remission is achieved by a DAS28 lower than 2.6 (comparable to the ARA remission criteria

Prognosis

The course of the disease varies greatly. Some people have mild short-term symptoms, but in most the disease is progressive for life.

Predictors of poor outcomes

1. Low functional score early in the disease

2. Lower socioeconomic status

3. Early involvement of many joints

4. High erythrocyte sedimentation rate or Creactive protein level at disease onset

5. Positive rheumatoid factor

6. Early radiologic changes

What a Patient should do?

- Exercise regularly.
- Lose weight if overweight.
- Eat a healthy diet.
- Use heat to reduce pain and stiffness (such as a hot shower or a beating pad).