REVIEW ARTICLE

REVIEW ON RHEUMATOID ARTHRITIS

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Abstract:
Rheumatoid arthritis is a chronic inflammatory disease characterized by severe-pain, swelling, stiffness and loss of function of the joint. It is classified as autoimmune disease characterized by deregulation of the immune system, deficit in Chronic activation of T-cell responses and over production of proinflammatory cytokines including Tumour factor and interleukin 1. It has been reported that genetic makeup of an individual plays an important role in determining the susceptibility of the person to developing rheumatoid arthritis. Infectious agents have long been suspected as potential triggers of RA. Researchers have not been able to identify any organism in the synovial tissue or bacterial nucleotide sequence in synovial tissues of RA patients.

Key Words: Rheumatoid arthritis, Proinflammatory cytokines, Aetiology, Pathology, Clinical manifestation, Management.

Introduction
Rheumatoid arthritis is a chronic inflammatory disease characterized by severe-pain, swelling, stiffness and loss of function of the joint. It is classified as autoimmune disease characterized by deregulation of the immune system, resulting in Chronic activation of T-cell responses and over production of proinflammatory cytokines including tumour necrosis factor and interleukin 1 (Reischmann et al., 2005). It is classified as autoimmune disease characterized by deregulation of the immune system, deficit in Chronic activation of T-cell responses and over production of proinflammatory cytokines including Tumour factor and interleukin 1 (Fleischmann et al., 2005). The resultant effect of the above response is joint destruction.

AETIOLOGY OF RHEUMATOID ARTHRITIS
The precise cause of RA is not known (Edward et al., 2006) disease models suggest that both genetic, environment and hormone are contributing factors. Firestein, in his publication classified the aetiology of RA as genetic, environment, hormone and socio-economic status.
It has been reported that genetic makeup of an individual plays an important role in determining the susceptibility of the person to developing rheumatoid arthritis. High rate of concordance between monozygotic twins and a ill-defined familial disposition has been reported (Silman et al., 1993) the association of human leucocyte antigen and DR4 with RA is well documented. There is an increased human of RA with this allele (Warrington et al., 2001). Many researchers have come to the conclusion that some environmental factors trigger the disease process in the people whose genetic makeup makes them susceptible to rheumatoid arthritis. There has been limited success in defining these factors, but recent work has suggested prenatal characteristics as important in the development of rheumatoid arthritis (Jacobson and Jacobson, 2003). Infectious agents have long been suspected as potential triggers of RA. Researchers have not been able to identify any organism in the synovial tissue or bacterial nucleotide sequence in synovial tissues of RA patients. Viral
PATHOLOGY OF RHEUMATOID ARTHRITIS

The earliest changes recorded in RA is swelling of the synovial membrane and the underlying connective tissue. The synovium becomes infiltrated with lymphocytes especially helper T cells, plasma cells and macrophages (Blab et al., 1999). Effusion of synovial fluid into the joint space takes place the active phase of the disease. Subsequently, hypertrophy of the synovial membrane occurs within the lymphoid follicles resembling immunologically lymph node. Inflammatory granulation tissue (pannus) is led spreading over and under the articular cartilage which is progressively eroded and destroyed (Firestein, 2001). This is red by fibrous adhesion which may form between the ross of pannus across the joint space and fibrous ankylosis occur in muscles adjacent the inflamed joint atrophy. There is a central area of fibrinoid material consisting of illen and fragmented collagen fibers, fibrinous exudates and cellular debris. The nodule is surrounded by a loose capsule of fibrous tissue. Similar granulomatous lesion may occur in the pleura lung pericardium and sclera lymph nodes are often hyperplastic showing many lymphoid follicles with large germinal centre and numerous cells in the sinuses of medullary cords. Immunofluorescence shows that the plasma cells in the synovium and lymph node synthesize rheumatoid factors.

CLINICAL MANIFESTATIONS OF RHEUMATOID ARTHRITIS

The onset of RA is insidious in majority of cases with joint pain, stiffness and symmetrical swelling of a number of peripheral joint (Brandtzaeq, 1997). Initially pain may be experienced only on movement of joints, but rest pain and especially early morning stiffness is characteristic of active RA. In the typical case the small joints of the fingers and toes are the proximal interphalangeal joint which gives the fingers a spindled appearance and swelling of the metacarpophalangeal joints resulting in broadening of the fore foot (Lipsky and crush, 1998). As the disease progresses with or without remission, it may spread to the wrist, elbows, shoulders, knees ankles, subtalar and metatarsophalangeal joints. The hip joints are affected only in the more severe cases, but, neck pain and stiffness from cervical spine involvement is common (Kelly et al., 1999). As disease progresses, pain, muscle spasm and progressive joint destruction which may cause limitation of joint motion takes place. Joint instability, subluxation and deformities may occur, which could be corrected at first but later permanent contratral develop and joint many become completely disorganized (Mccarty and koopman, 1993). This may result to anorexia, weight loss, lithergy and myalgia. Extra articular features include: Raynaud’s Phenomenon. Lympodenopathy, osteoporosis and many others (Gronzy, 2004).

Ocular manifestations include: Keratoconjunctivitis sica or dry eyes syndrome. This has been reported in 15 - 25 percent of patients. Others include scleritis or episcleritis which has been recorded in 4 to 10 percent of RA patients (Harper and Foster, 1998).

Cardiovascular manifestation may include asymptomatic pericarditis and rarely pericardial effusion vasculities may also manifest and presents as leucocotelasstic which may occur as Isolated skin finding with less common medium sized involvement.
Pulmonary manifestations in RA is mainly interstitial lung disease. Patients with severe RA or those who smoke are more likely to develop RA associated interstitial lung disease.

The most common haematologic manifestations of RA is mild anaemia with haematocrit values in the range of 30 - 34 percent. This has been recorded in 25 - 35 percent of patients. It is characterized by low concentration of serum iron and low serum iron binding capacity and does not respond to oral iron. The chronic anaemia may be complicated by true iron deficiency secondary to gastrointestinal blood loss from those treat with analgesic and anti inflammatory drugs (Denesi and Taccam, 2004).

White blood cells may be within the normal range or slightly elevated, but high counts have been recorded by past researchers. Increase in neutrophils has equally been recorded as well as raised basophil counts (Harrison, 2001). Leucopenia though very rare could be observed in a chronic state. There may be a shift to the left in neutrophilia. Eosinophilia has been reported in most studies. Felty's syndrome is characterized by neutropenia, often with anaemia and thrombocytosis, with splenomegaly and occasionally sedimentation rate is usually.

SOCIO-ECONOMIC IMPACT OF RHEUMATOID ARTHRITIS

By all measures, the financial and social impact of all types of arthritis including rheumatoid arthritis is substantial, both for the nation and individuals (Hallert et al., 2004). Economically, the medical and surgical treatment for rheumatoid arthritis and the wages lost because of disability caused by the disease add up to billions of dollars annually.

The total economic impact of RA in England was estimated at 1.2556 billion pounds due to production loss caused by RA disability (McIntosh, 1996). Daily joint pain is an inevitable consequence of the disease and most patients experience some degree of depression and feeling of helplessness. For some people RA can interfere with normal daily activities, limit job opportunities, or disrupt the joys and responsibilities of family life (Kevin, 2004). The excess mortality rate associated with RA has changed according to research work by (Gabriel et al., 2000). In recent analysis, the most common causes of death in patients with RA in the United State were cardiovascular, cancer and infection (Pincus, 2004).

DIAGNOSIS:

There is no unique test or feature that is pathognomonic for RA. Rather, the diagnosis is made by recognizing a pattern of signs and symptoms. A history consistent with the diagnosis of RA includes prolonged morning stiffness that may be improved by activity, polyarthralgias and/or polyarthritis, joint gelling, and fatigue. Examination findings that are suggestive of RA include: symmetric polyarthritis and rheumatoid nodules. Serologic and imaging studies may be helpful in excluding mimics of RA and confirming the diagnosis when pretest probability is high. Arthrocentesis is not diagnostic but is useful in excluding infection. Radiographic changes include periarticular osteopenia, and joint space loss. Although most serologic studies are not sensitive or specific for RA in general, the use of antibodies to cyclic citrullinated peptides (anti CCP antibodies) has recently been demonstrated to have specificity for RA in more than 90% of patients.

In patients with atypical presentation or when another diagnosis is equally likely (e.g., hepatitis C), anti-CCP antibodies may be useful in confirming the diagnosis of RA. (Saraux et al., 2003).

DIFFERENTIAL DIAGNOSIS:

The list of RA mimics is extensive. RA can resemble any disorder causing acute or chronic poly-arthritis. A thorough history and examination are often helpful in narrowing the differential diagnosis in the individual patient. Infectious arthropathies are an important consideration in the setting of fever and poly-arthritis. Infections frequently result in a transiently positive RF, so this is not helpful in differentiation. If bacterial arthritis is suspected, joint aspiration and synovial fluid cultures and blood cultures are often helpful in establishing the diagnosis. One exception is gonococcal arthritis, in which synovial cultures are often negative. Lyme disease is also associated with negative synovial fluid cultures and should be considered when a patient has been in an endemic region where tick exposure was likely (Hoving et al., 2004).

Viral infections, both acute and chronic, may result in a polyarthritis clinically indistinguishable from RA. Acute viral infection, such as parvirus B infection, often distinguish themselves by a history of exposure, an accompanying rash, and their self limited course.

Other connective-tissue diseases may manifest similarly to RA. Patients with systemic lupus erythematosus (SLE) may have a similar distribution of joint involvement but rarely have erosive disease. Jaccoud's arthropathy often leads to deformities that are similar in appearance to those in RA, but these changes result not from joint destruction.
but from tendon and ligament laxity. These deformities, unlike those in RA, are readily reducible on examination. In most cases, the other clinical manifestation of SLE and serologic findings are helpful in establishing the diagnosis. Psoriatic arthritis, when present without rash, may be difficult to distinguish from RA.

Involvement of the sacroiliac joints or the distal interphalangeal joints of the treatment regimens have significant overlap so, even when differentiation is not possible, instituting effective and appropriate treatment is not hampered. The other seronegative spondyloarthropathies (reactive arthritis, ankylosing spondylitis, Inflammatory bowel disease -associated arthropathy) can also closely resemble RA. Asymmetric joint involvement, the absence of small - joint disease, sausaging of digits, and the involvement of the lumbosacral spine all favour the seronegative arthropathies. Polymyositis and dermatomyositis may manifest with arthralgias, arthritis and joint stiffness, similar to RA. Muscle weakness and antibodies associated with these disorders most often readily distinguish these disorders from RA. Polyarticular crystal arthropathies may also mimic RA. Radiographs may also show joint erosions, but in calcium pyrophosphate dihydrate deposition disease, chondrocalcinosis is often apparent.

Synovial fluid analysis is diagnostic of crystal arthropathy. Polymyalgia rheumatica and giant cell arthritis may present with symmetric polyarthritis. In these cases; a detailed history may be helpful in identifying the characteristics of these disorders (e.g. a new unrelenting headache, predominant shoulder and hip girdle involvement), but in cases where this does not make the distinction, careful observation of the evolution of the disease over time, since the clinical courses and potential serious complication associated with these disorders are very different.

Systemic vasculitis may present polyarthritis and in the case of Wegener's granulomatosis, may also be RF - positive. Again a thorough history and examination with directed serologic and imaging evaluation will and in differentiating these disorders Chronic sarcoid arthropathy may clinically closely mimic RA, and on radiographs may show bony destruction similar to that in RA. Tissue biopsy may be necessary in these cases if no other manifestations of sarcoidosis are present to establish the diagnosis. Osteoarthritis is best differentiated from RA by a careful history and examination. The absence of systemic inflammatory signs and symptoms, onset in later life and the pattern of joint involvement are often enough to distinguish the two disorders. Erosive osteoarthritis may have an inflammatory appearance on examination, but it tends to involve the proximal interphalangeal joint primarily, is not associated with proliferative synovitis, is not RF-positive and – has a distinct radiographic appearance (Dixey et al., 2004) Ultrasonography is diagnosis of RA and is more sensitive in the detection of synovial and tendon inflammation than clinical examination alone. Ultrasonography may also be useful in guided joint aspiration and injection (Kane et al., 2003).

MANAGEMENT OF RA:

The mainstay of therapy in RA management is the use of Disease-modifying antirheumatic Drugs (DMARDs). These medications prevent or reduce joint destruction, maintain or improve function and in some cases, improve other aspects of the patient's general health. Glucocorticoids are used to suppress inflammation and preserve joint structure and thus may be considered as DMARDs. They are often used at disease onset or when disease flares results as a temporary aid in obtaining disease control. Because of their long-term side effects, it is desirable to obtain disease control without chronic use of GCs whenever possible and to use the lowest doses necessary. In a long action form, they are also useful for intra particular injection when only one or two joints are active. GCs in high doses are an essential part of treating organ threatening disease in RA, such as in rheumatoid vasculitis. They are also useful in maintaining disease control during pregnancy when most other DMARDs are contraindicated (Strong et al., 2004).

Methotrexate (MIX) should be considered first line therapy for the treatment of RA. MTX is a folic acid antagonist, but its precise mechanism of action in RA treatments is unknown. MTX acts within weeks to diminish disease activity. It has also been shown to decrease radiographic progression of disease. MTX can be used in combination With DMARDs to achieve and maintain disease remission.

Hydroxychloroquine and sulfasalazine are DMARDs that provide mild anti - inflammatory activity in most patients. They are used single agents (only in patients with very mild, non -erosive disease, or in combination. They are both well tolerated, with few side effects. Their major application in RA currently is as a supplement to MTX or other DMARD therapy. Leflunomide, a pyrimidine synthesis inhibitor, is also used as add - on therapy with MTX or other agents. Leflunomide may cause liver enzyme relavage and requires regular liver enzyme monitory (Hurliman et al., 2002).
Nonsteroidal anti-inflammatory drugs (NSAIDs) and analgesics should be used as symptomatic therapy only in combination with DMARD therapy in RA. These agents do not have any significant positive impact on disease progression or function. They should never be the primary or sole therapy in patients with RA (Edward et al., 2004).

Conclusion
Rheumatoid arthritis is a chronic inflammatory disease characterized by severe pain, swelling, stiffness and loss of function of the joint. It is classified as autoimmune disease characterized by deregulation of the immune system, deficit in Chronic inflammatory C-cell responses and over production of proinflammatory cytokines including Tumour factor and interleukin 1. Some scientists have suggested that a variety of hormonal factors may be involved in RA. The presence and activity of a number of proinflammatory chemokines and cytokins have established roles in disease pathogeneses. The earliest changes recorded in RA is swelling of the synovial membrane and the underlying connective tissue. The synovium becomes infiltrated with lymphocytes especially helper T cells, plasma cells and macrophages. Initially pain may be experienced only on movement of joints, but rest pain and especially early morning stiffness is characteristic of active RA. In the typical case the small joints of the fingers and toes are the proximal interphalangeal joint which gives the fingers a spindled appearance and swelling of the metacarpophalangeal joints resulting in broadening of the fore foot. The mainstay of therapy in RA management is the use of Disease-modifying antirheumatic Drugs (DMARDs). These medications prevent or reduce joint destruction, maintain or improve function and in some cases, improve other aspects of the patient's general health. Glucocorticoids are used to suppress inflammation and preserve joint structure and thus may be considered as DMARDs.

References


