Introduction & Aim of the work

Rheumatoid arthritis is a peripheral , symmetrical inflammatory polyarthritis with generalised connective tissue affection . It is characterised by prolonged morning stiffness, subcutaneous nodules, erosive joint changes in X-ray , high erythrocyte sedimentation rate and positive tests for rheumatoid factor in the serum (Curry, 1978).

The most useful guides to disease activity were determiend by analysis of blood and synovial fluid together with the history of joint disability (Farr et al.,1976).

In this study we assess clinically the disease activity and to measure the blood parameters including ;Erythrocyte sedimentation rate, Haemoglobin concentration, C - reactive protein , Total leucocytic count and rheumatoid factor and to measure the synovial fluid parameters including ; Glucose level, Rheumatoid factor , Total leucocytic count and polymorphs count and to determine which are related to the clinical parameters of disease activity.

RHEUMATOID ARTHRITIS

Rheumatoid arthritis is a peripheral symmetrical inflammatory polyarthritis with prolonged and distressing morning stiffness, Subcutaneous nodules, erosive joint changes in X - ray, elevated erythrocyte sedimentation rate and positive tests for rheumatoid factor in the blood with other laboratory evidence of chronic inflammation (Currey, 1978).

Although arthritis is the most frequent manifestation, rheumatoid arthritis is a generalised disease involving many systems, so that it would, more correctly be termed "Rheumatoid Disease" (Barnes & Mason, 1975).

Aetiology :

Although much has recently been added to our Knowledge about the aetiology of rheumatoid arthritis, the specific cause or causes of this disease still remains unclear. Intensive efforts have failed to establish that it is caused by a specific infectious agents, by nutritional disturbance, by faulty or unbalanced endocrine secretions, or by autonomic nervous system or somatic reflection of emotional disorders. Impressive evidence is accumulating to suggest the importance of an immunologic mechanism in the pathogenesis of the disease (Currey, 1978).

Infection :

Several groups of investigators reported the isolation of mycoplasma from both joint fluid and synovial tissues of patients with rheumatoid arthritis. These reports have not been substantiated by results from other laboratories. (Taylor et al., 1976). But it was found that an acute arthritis is followed by chronic polyarthritis when young yorkshire swine was given a single intraperitoneal inoculation of mycoplasma hyorhinis, antibodies showed a brisk response in both serum and synovial fluid. (Barden and Decker, 1971).

Duthie et al., (1976) have been able to isolate diptheroids from 30% of rheumatoid synovial membrane However, others have obtained similar results from non-rheumatoid joints and the evidence suggestis that these organisms do not themselves cause rheumatoid arthritis. They may just be passengers, or could play a role as immune adjuvants. (Currey, 1978).

Metablolic causes :

A number of apparent errors of metabolism have been found in patients with rheumatoid arthritis. They have been

concerned mainly with the heterocyclic amino acids tryptophan and histidine (Lawrence. 1970).

There is increased urinary excretion of tryptophan metabolites, tryptophan kynurenine and 3-hydroxy kynurenine, in patients with rheumatoid arthritis (Bett, 1964).

The metabolism of tyrosine appears to be abnormal in patients with rheumatoid arthritis (Robinson et al., 1962).

Immunological causes :-

Ziff, (1961) stated that connective tissue diseases possibly result from a genetically determined abnormality in the response of antibody forming cepls to normal self antigens.

Bartifeild (1969) accepted the altered immunological reactions as a definite causation in rheumatoid arthritis because of the existence of the macroglobulin (rheumatoid factor in the sera of patients with classic rheumatoid arthritis and the existence of soluble nucleoprotein antigen in synovial fluid of rheumatoid arthritis) much of the complement fixing activity of rheumatoid synovial fluid is associated with cryoprecipitate which is composed of Ig M, IgG antinuclear and complement Components. other immunoglobulis that were demonstrated in synovial fluids of rheumatoid arthritis are antibodies to native - DNA and anticollagen complexes. These immunoglobulis are mainly produced locally

in the diseased joints by plasma cells or B lymphocytes and studies had shown that immunoglobulins synthesis takes place in rheumatoid arthritis synovial membranes at rates comparable to those of lymph nodes and spleen.

In rheumatoid arthritis there are two types of lymphocytes:

B - Lymphocyte cells which represent the precursor of antibody - producing plasma cells (Dieppe et al., 1985).

T - lymphocyte cells which mediate the momocyte migration inhibitory factor in synovial fluid and response of antigen recogention.

The importance of these lymphocytes in the pathology of rheumatoid arthritis is indicated by a remarkable therapeutic improvement following depletion of thoracic duct lymphocytes (Williams et al., 1973).

The proportion of T/B cells in peripheral blood is normal in patients with rheumatoid arthritis (Clements et al., 1974) however in synovial fluid and tissue they are relatively higher (Sheldon et al., 1974).

The T cells have a major role in the pathogenesis of rheumatoid arthritis not only by the direct action of Killer cells (Monocyte migration inhibitory factor) but also through failure of suppressor cells (Messner, 1974).

Genetic factors :-

Recent discoveries of the relationship of histocompatability markers to the epidemiology of Certain diseases have indicated a strong genetic relationship of these cell surface molecules to apparant disease susceptibility. the associated molecules include those that are coded for the major histocompatability complex located on the human six chromosome (Sazasuki et al., 1977). It was found that there is a strong association between HLA - DW4 and rheumatoid arthritis. (Mc Micheal et al., 1977).

Endocrinal factors :-

The discovery of the remarkable ability of adreno-corticosteroids to suppress the inflammatory manifestations of rheumatoid arthritis stimulated an intensive search for an abnormality of adrenal or pituitary function. Such studies have been carried out and the majority suggest that while gross adreno - cortical secretory activity is apparently within normal Limits, but perhaps significant deviation from normal may occur. It is possible, though unproved, that such

small changes might provide a favourable enviroment in susceptible individuals for rheumatoid disease to manifest themselves by some independent process (Selye, 1951).

The hypothesis that an imbalance between hormones secreted by adrenal cortex or by pituitary gland was responsible for rheumatoid arthritis, has not been supported by clinical investigations or experimental studies (Robinson, 1974).

Psycho - somatic factors:

There is a widespread speculations concerning the role of a predisposing personality structure and of emotional trauma in the initiation and maintenance of the disease (Robinson, 1974).

A summary of the precepitating factors of rheumatoid arthritis by Short et al., (1957) showed that strain, mental, physical or both was the most common type of precepitents.

Pathogenesis of Rheumatoid Arthritis

The pathogenesis of rheumatoid arthritis may be considered in three definite stages :

a - Initiation of synovitis by an aetiological factor carried to the joint by the circulation.

b - Subsequent immunologic events that accentuates the primary inflammatory reaction in the synovium.

c - The transmission of inflammatory allergic reaction in the synovium to pannus formation (Zvaifler, 1979).

Antigen antibody complexes formed in the joint cavity activate the Complement system (Zvailer, 1974). Such an immune response in the synovial fluid Catalyses the activation of many processes which interact to produce a self sustaining active inflammation within the joint space. These include Complement, Kinins, clotting Factors, fibrinolysis. phagocytosis and lysosomes (Harris, 1981).

Dayer et al., (1976) showed that rheumatoid synovium secretes excessive amounts of Collagenases and prostaglandins especially prostaglandin E, which is Known to promote bone resorption (Kankrowitz et al., 1975).

It is the interaction of mononuclear cells that stimulates the synovium to proliferate and produce such proteinases and prostaglandins. (Harris, 1981).

As a result of such inflammatory process, the inflamed synovial villi become adherent to the adjacent margins of articular Cartillage and this adherent inflammatory tissue erodes the Cartilage as it creeps over it. This is called pannus (Vernon - Roberts, 1975), and by local release of its degradative enzymes it erodes both the Cartilage and subchondral bone. (Krane, 1974).

There is accumulation of polymorphnuclear leucocytes at the reaction site which plays an important role in inducing tissue injury (Perez and Weissmann, 1981). The exact cause of accumulation of these cells in the articular Cavity is unknown. It had been possible to detect certain chemotactic factors and agenerator of chemotactic activity in the synovial fluid of rheumatoid patients. (Ward and Zvaifler, 1970).

These polymorphnuclear cells phagocytose immune Complexes releasing lysosomal enzymes including elastase and Collagenase (Ohlsson, 1975). During phagocytosis some polymorphnuclear leucocytic cells die and are lysed releasing

proteinases and polysaccharides (Harris, 1981).

Cartilage and bone destruction occurs at the marigns of the bony ends. Recrucitment of perichondrial and periosteal cells as well as chondrocytes occurs in this destructive process (Mills, 1970). Tongues of proliferative cells penetrate the Cartilage and the destruction takes place in a very narrow Zone between the cells and the Cartilage (Harris et al., 1971).

Bone resorption necessitates demineralization of the bone as Collagenase and elastase can not degrade bone unless demineralised. This is carried out either by some inflammatory products which are able to mobilise bone minerals or by increased osteoclastic activity induced by prostaglandins. (Robinson et al., 1975).

Another mechanism for stimulating osteoclastic activity is the release of osteoclastic activating factor from mononuclear cells which accumulate in the rheumatoid synovium (Horton et al., 1974).