The Value of Isotope Scanning in Assessment of Joint Inflammation in Cases of Rheumatoid Arthritis

Thesis
Submitted for partial fulfillment of
The M.Sc. Degree in Internal Medicine

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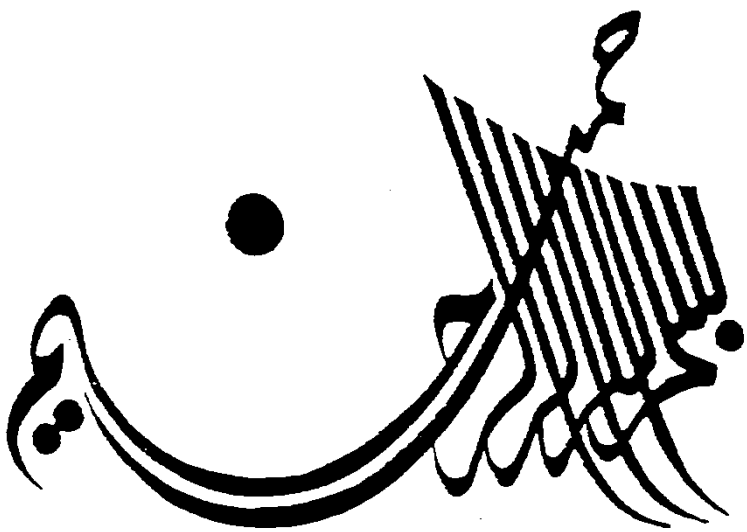

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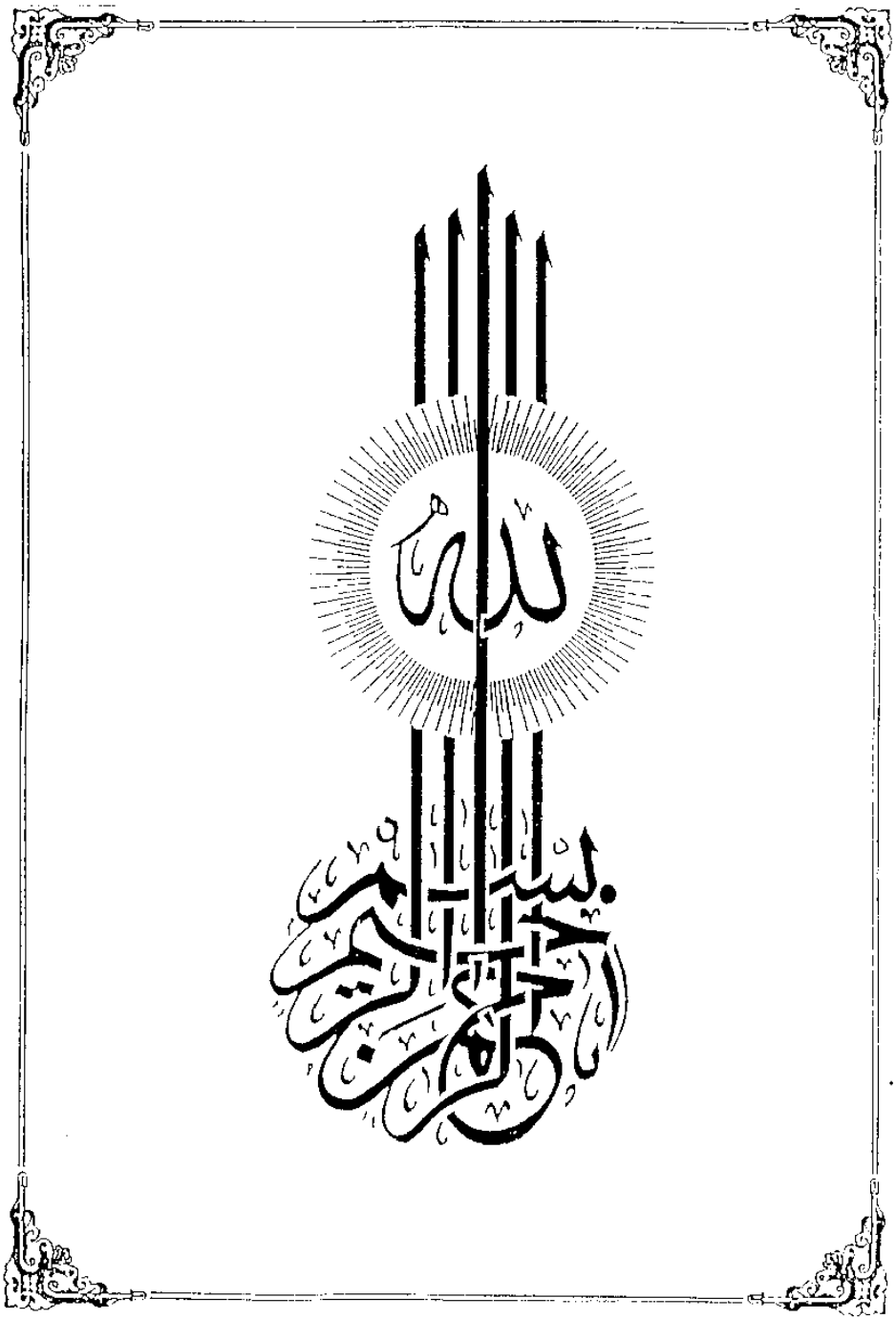

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Amina Badr El-deen

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INTRODUCTION AND AIM OF WORK

The Value of Isotope Scanning in Assessment of Joint Inflammation in Cases of Rheumatoid Arthritis

Introduction :-

Rheumatoid arthritis is the commonest form of chronic inflammatory joint disease. In its typical form rheumatoid arthritis is symmetrical, destructive and deforming polyarthritis affecting small and large peripheral joints. In about 25% of cases it may affect initially a single joint such as the knee joint. The assessment of joint inflammation is so far by clinical examination and x-ray. Recently, there are several radionuclides available for inflammation detection but one of their disadvantage is their lack of specificity. Non specific polyclonal human immunoglobulin G (HIG) labeled with ^{99m}Tc has been introduced as a more specific agent for localization of inflammation showing a high sensitivity and specificity. Some reports have suggested that ^{99m}Tc-HIG scintigraphy may be useful for detecting synovitis, and identifying joints with current active inflammation *Pons et al., (1993).*

Aim of the work :-

The aim of this study is to assess the validity of ^{99m}Tc-HIG joint scintigraphy as an objective test for detecting synovitis and its ability to distinguish between joints with and without active inflammation in chronic rheumatoid arthritis.

REVIEW OF LITERATURE

Rheumatoid arthritis

Definition :-

many different definitions were put for rheumatoid arthritis. It can be defined as a generalized connective tissue disorder involving extra-articular structures as well as joints *(Golding, 1982).*

But it can be defined better as a chronic, inflammatory, destructive and deforming Polyarthritis which predominantly affect females. It involves many different organs and therefore exhibits a wide spectrum of clinical manifestations and regarded as multisystem disease. Its etiology is unknown, but it is generally thought to be multifactorial involving immunological, genetic, environmental, and possibly viral factors *(Boulos et al., 1991).*

The prevalence of the disease is about 3% of the population. It is about 3 times as common in females as in males. There is increased evidence in those with family history of rheumatoid arthritis (5 - 10%) and an association with HLA DR4- (70%) *(Buchanan and Kean, 1986).*

The peak of incidence of rheumatoid in Egyptians occurs between 34 - 44 years of age *(El-Badaawy, 1979).*

Etiology of rheumatoid arthritis :-

Many hypothesises have been proposed to explain the etiology of rheumatoid arthritis.

• Genetic hypothesis :-

The prevalence of the disease in first degree relatives of patients with rheumatoid arthritis is 3 to 5 times greater than in normal controls *(Masson, 1979).*

In addition, certain histocompatibility antigens (HLA-DR_4, HLA-Dw_4) show strong association with rheumatoid arthritis; these data clearly point at a genetic component operating in this disease *(Deker et al., 1984).*

• Infective hypothesis :-

Sera from rheumatoid patients were examined for specific antibodies against some viruses; significant differences were observed as regards rubella, measles, and cytomegalo virus antigen as compared with healthy controls *(Kelly, 1989).*

Electron microscopic study of synovial cells from a rheumatoid joint revealed findings of cytomegalovirus in some cases. This fact proved some support for the Infective hypothesis *(Hummermann et al., 1982).*

• Vascular hypothesis :-

It was suggested by *Rithschild and Masi, (1982)* who stated that microcirculatory compromise, with an increase in metabolic needs of synovium, may initiate tissue injury via anoxia and local acidosis; resulting in release of hydrolytic enzymes, increase vascular permeability and accelerate the inflammatory process.

• Endocrinal hypothesis :-

There is no known endocinal abnormality consistently occurs with rheumatoid arthritis, but it was noticed that it has higher incidence in females, and probably lower in those taking contraceptive pills, with remission common in pregnancy, exacerbations common during menopause. Also, arthritis resembling rheumatoid may occur in acromegaly. Adrenocortical steroids and ACTH produced marked decrease in the disease activity *(Goldoiing, 1982).*

• Metabolic hypothesis :-

Patients with rheumatoid arthritis have many errors of metabolism of the amino acid tryptophane and histidine. There is increase in urinary excretion of tryptophane kynurenine and 3-hydroxy kynurenine which correlates with a high turn over of fibrinogen *(Lawrence, 1970).*

• Autoimmune hypothesis :-

This is, so far, the most accepted theory implying that the central fault is an abnormal immune reaction directed against some body components *(Bennett, 1981)*.

Rheumatoid synovitis is associated with the presence of immune complexes within the joint space, these complexes activate the complement system and thus cause chemotaxis of polymorph nuclear cells which in turn, phagocytose the immune complexes and release lysosomal enzymes which are the immediate cause of synovitis *(Zvaiflar, 1979)*. It was also found that sera of many rheumatoid patients have high levels of circulating immunoglobulin (rheumatoid factor), occasional antinuclear factors, which frequently precede the onset of clinical disease *(Golding, 1982)*.

Pathogenesis of rheumatoid arthritis :-

Rheumatoid arthritis is considered to be both an extravascular immune complex disease and a disorder of cell mediated immunity leading to inflammation, granuloma formation, and joint destruction *(Zvaiflar, 1979).*

This occurs through the following sequence ;

Localization of unidentified antigen in joint and local synthesis of antiglobulin antibodies. The antigen-antibody complexes formed in the joint cavity in turn, activate the complement system within the joint. Such response catalyses the activation of neutrophils chemotaxis, cytolysis, lymphokins production, kinins production and macrophage enzymes release. All these processes interact to produce a self sustaining active synovitis *(Deker, 1984).*

The interaction of mononuclear cells stimulate the synovium to proliferate and to secrete excessive amounts of collagenase enzyme and prostaglandin E which is known to promote bone resorption *(Harris, 1981).*

The polymorph-nuclear leukocytes which infiltrate the synovium in early stage of rheumatoid arthritis, phagocytose immune complexes, releasing pro-inflammatory prostenoides, oxygen radicals, and leukotrienes which interact synergistically with other mediators to produce vasodilatation, edema, heat and loss of function. Moreover, the monokine

interleukin 1 (IL-1) is found in increased concentration in rheumatoid arthritis synovial fluid and contributes to inflammation. IL-1 interacts with substance P, that is released into the inflamed joint. The latter, in turn, activates macrophages to secrete oxygen radicals, prostenoids and increase the amount of IL-1 *(Fassbender, 1986).*

If untreated rheumatoid synovitis becomes a self perpetuating process, the predominating neutrophilic infiltration of the synovium is replaced by lymphocytes (70-75% of the T-lymphocyte type), plasma cells, fibroblasts, and macrophages while in synovial fluid, millions of polymorph-nuclear leukocytes accumulate as the immune response is established *(Menninger et al., 1980).*

As a result of such inflammatory process, the inflamed synovial membrane becomes adherent to adjacent margins of articular cartilage and this adherent inflammatory tissue erodes the cartilage as it creeps over it; this called pannus *(Krane, 1974).*

Pathology of rheumatoid arthritis :-

Pathology of rheumatoid arthritis is described by considering synovitis, anatomical consequences of the primary synovial lesion, and changes in composition of synovial fluid *(Stephen and Lee, 1986).*

Synovitis is the essential pathology of rheumatoid arthritis, including three pathological elements, which are exudation, cellular infiltration, and granuloma formation. Exudation as a result of congestion and edema of the synovium leading to effusion into the joint space *(Sokoloff, 1979).*

Cellular infiltration of the highly vascular synovium leads to perivascular infiltration by excess lymphocytes and plasma cells *(Barnes and Mason, 1975)*, however, earlier changes in synovium include hyperplasia of the lining synovial layers and infiltration with mononuclear cells and few polymorphs *(Deker et al., 1984).*

In addition, proliferation of blood vessels, synovial cells and fibroblasts in areas of cellular infiltration leads to formation of granulation tissue. The thick vascular synovial membrane or pannus becomes adherent to the cartilage and releases its degenerative enzymes which play an important role in the joint cartilage destruction *(Sokoloff, 1979)* and bone resorption *(Takahashi, 1983).*

In the subchondral bone, an inflammatory reaction similar to that in synovial tissue is found although numbers of osteoclasts are present.