Original Article

Cardiac Manifestations In Patients Of Rehumatoid Arthritis

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Abstracts: Cardiovascular manifestations of Rheumatoid arthritis have never been studied before therefore this study was designed to evaluate cardiac disease in patients suffering from rheumatoid arthritis.

Methodology: Fifty patients of Rheumatoid Arthritis presenting in Out Patient, Emergency and Rheumatology Clinic of Mayo Hospital Lahore from March 1998 till January 1999 were studied. All of them full filled the criteria for the diagnosis of Rheumatoid Arthritis as described by the American Rheumatism Association. After history and physical examination, a clinical assessment of the patient was made of whether he / she had Cardiac Manifestations of Rheumatoid Arthritis or not.

Results: Out of 50 patients seen 35 were female, and 15 were male. Giving a female to male ratio of 2.3 to 1. Maximum number of patients seen were between 26 45 years i.e 31(62%) In which 19 (38%) were between 26 to 35 years and 12 (24%) were between 36-45 years. Next most frequent group was of 8(16%) patients, between 15-25 years of age. Short systolic murmurs were heard in four patients. One patient showed pulsus paradoxus while in the rest no rhythm irregularity was felt. Myocarditis or Coronary Rheumatoid disease was not noticed in any patient. No heart block of any degree was seen. In 4 E.C.G's low voltage was demonstrated in the limb leads. Out of 50 Patients only 3 had pericardial effusion. In one patient it was only a thin rim more prominent posteriorly than anteriorly.

Conclusion: Cardiac manifestations of Rheumatoid Arthritis also occur in Pakistani Population, although not with the same frequency as in the Western world. It is also concluded that in Pakistani population, like in the West, the most common Cardiac complication is Pericardial Effusion.

Keywords: Rheumatoid arthritis, Cardiovascular disease, ischemic heart disease, Pericardial effusion

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease that leads to progressive joint deformity, disability and premature death.[1-6] Premature deaths in RA patients are due to increased cardiovascular disease (CVD), including ischemic heart disease (IHD) and cerebrovascular accidents (CVAs). Increasingly, it has been recognized that inflammation plays an important role in atherosclerosis,[7,8] making the evaluation of death from cardiovascular causes and RA all the more important, because inflammation is such an intrinsic component of RA.[6]

Data from population- and clinic-based epidemiologic studies of rheumatoid arthritis patients suggest that individuals with rheumatoid arthritis are at risk for developing clinically evident congestive heart failure. Many established risk factors for congestive heart failure are over-represented in rheumatoid arthritis and likely account for some of the increased risk observed.[9]

The incidence of CHF increases with age;[10,11] 88% of affected individuals are over the age of 65 years, and 49% are over 80 years at diagnosis.[10] The remaining lifetime risk of developing CHF at all index ages from 40 through 80 years of age is between 20% and 33%, and is roughly equal for men and women.[12,13]

Wolfe et al[14] reported an Factors associated with prevalent and incident CHF were those typically associated with CHF in the non-RA population (e.g., age, male gender, hypertension, coronary artery disease, diabetes, and smoking) while RA-related measures (patient-reported disability, pain, and RA global severity) were also associated with prevalent and incident CHF.[14]

Systemic hypertension is one of the most potent risk factors for CHF, conferring a two- to three-fold increase in CHF risk for affected individuals.[15]

Myocardial infarction (MI) is the most potent risk factor for CHF, with a population-attributed risk for

The development of CHF in the Framingham cohort of 34% for men and 13% for women.[15]
Several studies have confirmed an approximately two- to fourfold increase in risk for MI among RA patients compared to non-RA controls.[14,16,17]
RA hearts have identified an increased prevalence of granulomatous and non-granulomatous valvular abnormalities, particularly of the mitral valve, and an increased prevalence of mitral regurgitation in RA patients compared to matched non-RA controls. No longitudinal echocardiographic studies have been performed, however, to determine the impact of this finding on the subsequent risk for developing CHF in affected RA patients. Destructive valvular lesions leading to complete valvular incompetence have been reported but are considered rare occurrences.[18,19] In Pakistan cardiovascular manifestations of Rheumatoid arthritis have never been studied before therefore this study was designed to evaluate cardiac disease in patients suffering from rheumatoid arthritis.

Patients and Methods

Fifty patients of Rheumatoid Arthritis presenting in Out Patient, Emergency and Rheumatology Clinic of Mayo Hospital Lahore from March 1998 till January 1999 were studied.
All of them full filled the criteria for the diagnosis of Rheumatoid Arthritis as described by the American Rheumatism Association.
A detailed history was taken with special attention towards complaints suggestive of cardiac involvement. A thorough physical examination was done with extra attention towards Rheumatoid nodules and Cardiovascular signs.
After this a clinical assessment was made of whether the patient had cardiac manifestation of rheumatoid arthritis or not.
Following investigations were carried out to determine patient's condition, his Rheumatoid score, and if there was any cardiac involvement:

1. Rheumatoid Arthritis factor. If found positive when possible titers were also done.
2. Radiograph of the involved joints.
3. Hb, T.L.C., D.L.C.
4. E.S.R
5. Platelet count.
6. Blood urea.
7. Serum Creatinine.
8. Fasting Blood Surgar.
9. Liver function tests. (Bilirubin, direct and indirect, S.G.O.T., SG.P.T Alkaline phosphatase).
10. Serum Uric Acid (if required)
11. Complete examination of urine.

Results

A total of 50 patients were seen, in all of them the diagnosis of Rheumatoid Arthritis was established after this Cardiac status was examined.
Out of 50 patients seen 35 were female, and 15 were male. Giving a female to male ratio of 2.3 to 1. Maximum number of patients seen were between 26 45 years i.e 31, (62%) In which 19 (38%) were between 26 to 35 years and 12 (24%) were between 36-45 years. Next most frequent group was of 8 (16%) patients. Between 15-25years.
Of the 15 Male patients seen the youngest was 25 while the oldest was only 41. While in case of female patients the youngest was only 18 years of age and the eldest was 77 years old.
Out of the 19 patients examined, between the age group 26-35, 11 were female and 8 male giving a ratio of 1.4 to 1 While in the age group of 36-45 , 6 were female and 6 were male thus a ratio of 1:1. In the age group of 15-25 7 were females and I male.
In rest of the age groups only female patients were seen.
RA factor was positive is 43(86%) patients and negative in 7 (14%).
Of the 43 positive patients 30 were female, and 13 male. Thus a ratio of 2.3 to 1, similarly of the 7 RA factor negative patients, 5 were female and 2 male, so a ratio of 2.3: 1.
All the 50 patients were diagnosed and scored according to the criteria described by the American Rheumatisum association -1988 revision.
In all of these patients the first four criteria were present with a duration of more than sex weeks. i.e.

a. Morning stiffness of more than one hour duration.
b. Arthritis of 3 or more joint areas.
c. Arthritis of hand joints.
d. Symmetrical arthritis.

Variation of score resulted because of the 3 R' s i.e.

I. Rheumatoid factor.
II. Radiological changes
III. Rheumatoid nodule.

A score of 4 was seen in only 2 patients. 5 was scored by 14 patients. Out of these 14, 5 were R.A factor negative with radiological changes while 9 hand R.A. factor positive but no radiological change. In 34 patients the score was 6. Rheumatoid module as not seen in any patient thus no one had the score of 7.
Of the 50m patient seen, 11 did not have any

radiological change.
Thirty nine patients who showed radiological changes the least common was periarticular Osteoporosis noted only in 4 patients, while the most common was Periarticular Osteoporosis along with loss of articular cartilage reduction in joint space-observed in 17 patients. The stage of erosion was seen in 9 patients and the end stage i.e. of subluxation and ankylosis was noted in 10 patients.
Of the 50 patients seen 22 (44%) had symptoms for 1-5 years. The next most common groups was of 6 months to 1 year of 10 patients and of 9 patients between 5 year to 10 years. The average duration of the symptoms was 4 years 7 months.
Out of the 50 patients seen, there were only 8 (16%) patients who definitely had not used steroids. It is worth noting that the symptoms of arthritis in all these 8 patients had not been for more than one year.
On the other hand of the 37 patients who had symptoms of Rheumatoid Arthritis for more than one year 30 had a definite history of use of steroids.
Most of the patients noted had presented in our units Rheumatology Clinic. Only 10 (20%) had present in Outpatient Department while only 2 (4%) had such severe arthritis that they had presented in the Casualty and Emergency Department.
Our of the 50 patients seen only 11 needed admission due to severity of arthritis or some other medical reason.
After history and physical examination, a clinical assessment of the patient was made of whether he / she had Cardiac Manifestations of Rheumatoid Arthritis or not.
Out of 50 patients there was a strong suspicion of pericardial effusion in one and not so strong in another.
Short systolic murmurs were heard in four patients.
One patient showed pulsus paradoxus while in the rest no rhythm irregularity was felt.
Myocarditis or Coronary Rheumatoid disease was not suspected in any patient.
No heart block of nay degree was seen.
In 4 E.C.G's low voltage was demonstrated in the limb leads.
Out of these 4 , 2 had low voltage i.e. less than 0.5 mV in al the six limb leads. One patient had low voltage in 5 limb leads. One patient had low voltage in 4 limb leads and 0.6 mV in 2 limb leads.
Later it was observed that pericardial Effusion was responsible for low voltage in all the six limb leads in one patient, and also in another patient who had low voltage in 4 of the 6 limb leads. Low voltage in all the limb leads in the other patient was attributed to the thick chest wall. While in the fourth patient no definite reason for low voltage in 5 of the 6 limb could be determined.
Out of 50 patients examined cardiothoracic ratio on X-Ray Chest P-A view was found more than 1:2 in only 6 patients. Out of these, the heart's shape was globular in only 2. Later it was seen that both had pericardial Effusion.
Out of 50 Patients only 3 had pericardial effusion. In one patient it was only a thin rim more prominent posteriorly than anteriorly. Pericardial tap was not done due to small amount of fluid.
The pericardial effusion in the other two was of sufficient quantity that they could be safely tapped.
One patient refused and was managed conservatively. Second echocardiography on this patient after one month showed that the fluid had slightly decreased.
Pericardial effusion was tapped in the third patient. It was a transudate with low sugar and R.A factor positive. After one month of treatment and tap a thin rim of effusion was seen only posteriorly on echocardiography.
No valve abnormality was seen on echocardiography.
All chambers and L.V. function were with in normal limits.
How ever in 3 patients 1 or 2 small segments of pericardial thickening were noted.
These thickenings were not considered to be of any significance.
Out of the 50 patients seen, Pericardial Effusion was noted in 3 patients. It was proven to be secondary to Rheumatoid Arthritis in only I patient. In the other 2 it was strongly suspected to be secondary to Rheumatoid Arthritis, other reasons especially tuberculosis was ruled out.
No valve lesion or heart block was seen. No diagnosis of Myocarditis of Coronary Arteritis secondary to Rheumatoid Arthritis was made.

Discussion

Rheumatoid Arthritis a chronic systemic, inflammatory, connective tissue disease is mainly known as a disease affecting the diarthroidial joints which usually has a symmetrical involvement. However this disease has serious extra-articular complications too. This disease in it's natural course can take up a variable clinical progression.[20]
A patient of Rheumatoid Arthritis who has Cardiac Manifestations may present after a long and protracted illness, or cardiac manifestation of this disease may even be it's presenting feature.[21]

The average duration of disease of Rheumatoid Arthritis in all cases was 4 years and 7 months, with female to male ratio of 2.3 to 1. In the current study it was noted that the individuals who developed Pericardial Effusion had the disease for an average 10 year with female to male ration of 2 to 1. This was consistent with the 3.5 to 10 year reported by Kirk et al.[22]

No patient developed cardiac tamponade. Pericarditis is the most common cardiac manifestation of Rheumatoid Arthritis.[23] This is supported by various reports e.g. by Esclante et al[24], and Stollerman et al.[25]

In this study of 50 patients, Pericardial Effusion was seen in 3 patients. This was the most common Cardiac Manifestation of Rheumatoid Arthritis in the disserter's group of patients also. In all these patients this disease had produced grade 4 radiologi8cal changes of the joints affected. Other Extra-articular manifestations, besides the heart, were also seen. Out of these 3, 2 had Scleritis, all had G.I symptoms (these could even be due to N.S.A.I.D.). One patient who had the illness for more than 12 years, also complained of distal neuropathy. At the time of presentation the markers of disease activity were elevated i.e. E.S.R., C.R.P., Platelet Count, etc. It has been pointed out by Cosh et al[21], that their was no specific relationship between disease activity and pericarditis, but broadly speaking it is more common in advanced active disease.

The diagnosis of pericardial Effusion after clinical examination was only in one case. While after investigations especially Echocardiography where one can "See" the Effusion was in Three.

One reason for the low incidence documented in the Pakistani Population could be that in none of these patients Rheumatoid Nodule was seen. Incidence of pericardial Effusion with Rheumatoid Nodule is higher.[21,25] Secondly the average duration of illness in our cases was only 4 year and 7 month where as Cardiac complications manifest in many patients of longer duration.[22]

Pericardial Effusion could only be tapped in one patient (One patient refused and the other had a very thin rim mainly posteriorly which could not be tapped). Results of the tap showed R.A Factor positive with low sugar level findings consistent with Rheumatoid Effusion.

Pericardial Effusion was tapped by the Sub-Xiphisternal approach. This was a diagnostic-therapeutic procedure. There were no complications during or after the paricardiocentesis. Echo- cardiography after one month showed only a thin rim of fluid with no further re-accumulation.

Non-specific E.C.G changes were seen in 4 patients, None of these E.C.G.'s showed any evidence of Heart Block or Myocardial Infarction. E.C.G done after one month in the patient whose pericardial tap was done, showed increased voltage. Arthritis of these patients limited us from performing an exercise test to elicit Heart Block.[21]

On Doppler Echocardiography a mild Aortic Regurgitation was seen in only two patients. Also Doppler Echocardiography showed in one patient, mild Mitral regurgitation. None of these patients had may other Cardiac finding (Valves were normal in patients who had Pericardial Effusion).Final diagnosis for these regurgitations could not be established, as this could only be done on Biopsy of the valve. In patients of this study the valve functions were sufficiently good and did not require replacement or repair.

The diagnosis of Myocarditis which was seen in nearly 19% of autopsies[25] was not suggested in any of these patients. In all of these patients both the Ventricles was normal, and did not suggest Myocarditis.[26,27] Also since their was no Heart Block Myocarditis was further ruled our as a possibility.[21]

Coronary Arteritis is a feature of sero-positive, nodular, erosive Rheumatoid Arthritis. None of the fifty patients had Rheumatoid Nodule and neither did any E.C.G showed any evidence of Myocardial Infarction or Heart Block. Thus no patient of Coronary Arteritis was either seen.

Conclusion

Cardiac manifestations of Rheumatoid Arthritis also occur in Pakistani Population, although not with the same frequency as in the Western world. It is also concluded that in Pakistani population, like in the West, the most common Cardiac complication is Pericardial Effusion. While the other Cardiac Manifestations of Rheumatoid Arthritis are also rare in Pakistan as in the West.

To get a better assessment of the incidence of Cardiac Manifestations of Rheumatoid Arthritis, autopsy is essential. In our social set up this is rather difficult so to find out the exact incidence and type of Cardiac manifestations of Rheumatoid arthritis in Pakistani Population is not possible at present.

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CORRIGENDUM

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In Original Article,
"A Study Comparing Artemether and Quinine in Adults with Severe Falciparum Malaria"

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Page No. 11, (tables 1, 3) should be read as (tables 1, 2).

Page No. 12, table 3 should be read as follows:

Table-3 Assessment of recovery after treatment with artemether or quinine.

Variables	Artemether	Quinine	P Value
Parasite clearance time in days (mean±S.D)	3 ± 3	4 ± 2	NS
Fever resolution time in days (mean±S.D)	5 ± 3	4 ± 2	NS
Time to recovery from coma in days (mean±S.D)	3 ± 2	2 ± 1	NS
Duration of hospitalization in days (mean±S.D)	10 ± 3	8 ± 3	NS