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Original Article

Increased prevalence of subclinical atherosclerosis in ankylosing spondylitis

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ABSTRACT

Objectives: The increased risk of atherosclerosis in inflammatory rheumatic diseases like rheumatoid arthritis and systemic lupus erythematosus has been established in various studies. However, similar studies in ankylosing spondylitis (AS) have yielded conflicting results. We studied subclinical atherosclerosis and endothelial dysfunction sonographically in AS patients and compared the results with matched healthy controls.

Methods: Fifty AS patients and 50 age and sex matched controls were recruited. However, 45 AS patients (28.6 ± 8.2 years; 42 males and 3 females) and 42 healthy controls (29.6 ± 8.6 years; 38 males and 4 females) were studied, as the others were excluded because of dyslipidemia. Height, weight, and waist circumference measurements were taken. Flow-mediated dilatation (FMD) of the brachial artery, intima-media thickness of the common carotid artery (CIMT) and ankle-brachial index (ABI) were measured sonographically.

Results: AS patients had significantly higher CIMT compared to controls (0.56 ± 0.1 mm in AS patients and 0.51 ± 0.08 mm in controls; $p = 0.03$). FMD was lower in AS patients (14.1 + 9.7%) as compared to controls (18.1 + 8.7%; $p = 0.04$) and ABI was higher in patients (1.16 + 0.1) as compared to controls (1.1 + 0.1; $p = 0.05$) 20% of AS cases had impaired FMD (defined as a FMD <4.5%) compared to none among the controls ($p = 0.03$).

Conclusions: This study revealed an increased prevalence of subclinical atherosclerosis in AS patients.

1. Introduction

Ankylosing Spondylitis (AS) is a chronic inflammatory disorder of unknown etiology predominantly involving the axial skeleton. The prevalence of AS in the general population varies between 0.2 and 0.9%.[1] AS is not an uncommon disease, indeed, almost 5% of patients with low back pain have AS.[2]

AS patients have mortality rates approximately 1.5–1.9 times than that of the general population.[3] Although most of this excess mortality is due to cardiovascular causes (20–40%),[4] the well-known cardiac manifestations of AS (like aortic regurgitation, heart block, etc.) alone cannot explain

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this phenomenon. Recent studies have shown that the chronic inflammation associated with AS may produce many varied and significant changes in multiple organ systems throughout the body including the cardiovascular system, and these changes may contribute to the increased mortality and morbidity associated with it.[5]

In a cross sectional study of 1843 AS patients it was found that the prevalence of atherosclerosis was 1.5 times of that of the general population.[6] Although this study also found a higher prevalence of well-known risk factors of atherosclerosis like diabetes mellitus, hypertension and hyperlipidemia in AS patients, the possibility of a contribution from the chronic inflammatory state of AS towards the pathogenesis of atherosclerosis cannot be ruled out. The increased risk of atherosclerosis in inflammatory rheumatic diseases like systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and anti-phospholipid antibody syndrome (APS) has been well defined through various studies and has been at least partly attributed to inflammation.[5] However, the evidence linking the inflammatory process in AS to atherosclerosis is contradictory.[7–12]

2. Materials and methods

Our study was a single centre cross sectional study conducted in the out-patient Rheumatology clinic of the All India Institute of Medical Sciences, New Delhi. After obtaining the approval of the study protocol by the institute's ethical committee, fifty consecutive patients of AS and an equal number of healthy controls were recruited between July 2008 and December 2009. Written informed consent was obtained from all the subjects. All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 1983.

2.1. Selection of patients

All AS patients were diagnosed according to modified New York criteria.[13] They were above 18 years of age and had disease duration of at least 2 years. We excluded subjects who had been already diagnosed with diabetes mellitus,[14] hypertension,[15] hyperlipidemia (on lipid lowering drugs), coronary artery disease (abnormality in electrocardiogram, echocardiogram or coronary angiography), peripheral vascular disease (confirmed by doppler or angiography), cerebrovascular disease (confirmed by computerized tomography scan or magnetic resonance imaging of the brain), renal insufficiency (defined as serum creatinine >1.2 mg/dL) or hypothyroidism (TSH >4 micro IU/mL or as a person on oral thyroxine supplements).

2.2. Clinical assessment

A detailed history was recorded from the patients regarding the disease duration, sites involved and the drugs used. The joints and entheses involved in the disease process were assessed for swelling and pain. Height and weight of the patient were recorded. Waist circumference was taken midway between lower border of the rib cage and the iliac crest. Chest expansion was measured in centimeters as the difference between maximal inspiration and maximal forced expiration at the level of nipples in males and just below the breasts in females. Blood pressure was recorded by a sphygmomanometer. Patients who had a systolic BP >140 mm Hg and a diastolic BP >90 mmHg were classified as hypertensive according to the JNC-7 criteria[15] and excluded. All the peripheral pulses were assessed and both the carotid arteries were auscultated for bruits.

2.3. Bath indices

Spinal mobility was assessed using the Bath Ankylosing Spondylitis Metrology Index (BASMI).[16] Lateral lumbar flexion, tragus to wall distance, lumbar flexion measured by modified Schober's test, maximal intermalleolar distance and cervical rotation were the criteria employed to assess spinal mobility. Disease activity was evaluated with the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).[17] Functional status was evaluated using Bath Ankylosing Spondylitis Functional Index (BASFI).[18] All the indices were scored in a scale ranging from 1 to 10.

2.4. Selection of control group

50 volunteers (patient's friends or hospital staff) matched for age, sex and smoking status were recruited and served as controls. None of them had a family history of AS, psoriasis, psoriatic arthritis, RA, SLE or any other inflammatory rheumatic disease. None of them had been diagnosed with diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, peripheral vascular disease, cerebrovascular disease, chronic renal failure or hypothyroidism at the time of study.

2.5. Laboratory examination

After an overnight fasting of at least 8 hours venous blood sample was obtained for the measurement of serum concentrations of total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), Very low-density lipoprotein (VLDL), triglycerides and C-reactive protein (CRP), erythrocyte sedimentation rate (ESR). CRP was done using immunoturbidometry method (CRP Turbilatex, Reliable Medical Supply & Co.). ESR was done using Wintrobe's method.

2.6. Radiographic assessment

2.6.1. X-ray

Plain X-ray pelvis anteroposterior view was used to assess sacroiliitis which was graded according to the Modified New York criteria[13] by a single observer (SG).

2.6.2. Ultrasonic measurement of the surrogate markers of atherosclerosis

All ultrasound measurements were taken in a quiet, temperature controlled room at the same time of the day (between