ORIGINAL ARTICLE

Utility of 99mTc-MDP Bone Scan in Comparison to MRI and Plain Radiographs for the Diagnosis of Early Spondyloarthropathy

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ABSTRACT

Introduction: Spondyloarthropathy as a cause of inflammatory lower back ache often goes undiagnosed for long. Though various clinical criteria have been developed, evidence of sacroiliitis is considered the basis for diagnosis. As sacroiliitis may become apparent on plain radiographs after a long duration, it is important to evaluate the efficacy of other imaging techniques to make an early diagnosis. Magnetic resonance imaging (MRI) and development of various specific sequences have helped in picking up structural changes as well as inflammation in sacroiliitis. The present study is to assess the role of MRI and radionuclide bone scan in patients with early SpA of less than 3 years.

Materials and methods: Patients with inflammatory LBA, defined according to the Calin criteria and satisfying the European Spondyloarthropathy Study Group (ESSG) criteria for SpA of less than 3 years duration, were included. Controls had mechanical LBA. A detailed clinical assessment and assessment of disease activity and functional impairment was done with validated measures. Radiological assessment included conventional radiograph of the pelvis, radionuclide scan and MRI of sacroiliac joints (SI joints). The sensitivity, specificity and predictive value of each modality in contributing to the diagnosis of SpA were assessed.

Results: Assessment of 136 SI joints in 42 patients [(Age 29 ($\pm$ 5.6) and 26 controls (Age 32.1 ($\pm$ 8.91)] was done. The mean disease duration of cases was 12.5 ($\pm$ 10.2) months. Conventional radiograph failed to pick up sacroiliitis in any of the cases. Positive bone scan was present in 34 cases (28 bilateral sacroiliitis, 6 unilateral sacroiliitis). Bone scan had a sensitivity of 81.8% and a specificity of 87%. Magnetic resonance imaging abnormality was present in 37/42 (88%) (bilateral in 27 and unilateral in 10) and in none of the controls. This accounted for a sensitivity of 87% and a specificity of 100%. The MRI changes included bone marrow edema (82%), synovial enhancement (60%), subchondral edema (42%), erosions (46%) and sclerosis (38%).

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Conclusion: In patients with early SpA of less than 3 years duration, conventional radiographs did not pick up sacroiliitis; however, both the radionuclide scan and MRI were useful.

Keywords: Sacroiliitis, Bone scan, Spondyloarthropathy, MRI, 99mTc-MDP, SPECT CT, Two phase.

INTRODUCTION

Spondyloarthropathies (SpAs) are a complex group of disorders characterized by chronic inflammatory disease of the axial skeleton with certain common clinical features, genetic predisposition and radiological features of sacroiliitis.[1] Most diagnostic criteria revolve around radiological evidence of sacroiliitis as an important component of ruling in SpA. However, it is important to note that early sacro-iliitis is often not visible on conventional radiographs, which may lead to a long delay in establishing a diagnosis. In fact a study reported a mean duration of more than eight years between the start of symptoms and the diagnosis of anky-losing spondylitis (AS).[2] The delay could have an important therapeutic implication as tumor necrosis factor-α (TNF-α) blocking agents, if instituted early in the disease, have a good efficacy and ability to modify the natural history of these disorders.[3-5] Magnetic resonance imaging (MRI) has been shown to be a promising modality for the detection of sacroiliitis in early SpA.[6,7] Radionuclide scintigraphy or bone scan has been around for many decades and has also been utilized despite its inherent limitations, for diagnostic evaluation of SpA. In our study, we tried to assess the role of MRI as compared to radionuclide scan and plain radiographs in the diagnosis of early SpA.

MATERIALS AND METHODS

The study was conducted at Kovai Medical Center and Hospital, Coimbatore; a large tertiary care hospital in South India. Patients from the rheumatology or orthopedic OPD with inflammatory low back pain, defined according to the

Calin criteria and satisfying the European Spondyloarthropathy Study Group (ESSG) criteria, were included (Table 1).[8,9]

The Calin criteria comprise four of the following five criteria, namely back pain of insidious onset that persists for at least 3 months, age of onset before 40 years associated with morning stiffness and that improves with exercise. Only adult patients between the age of 18 and 46 years, with a disease duration of less than 3 years were included. Controls were included from patients presenting with LBA and having an established diagnosis to explain the pain, like prolapsed intervertebral disk, spondylolisthesis, metastases, etc. Informed consent was taken from all. A clinical history of joints involved was taken and examination of musculoskeletal system done. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) assessment was done and erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) and HLA B27 status evaluated.[10] Radiological assessment included plain radiograph of SI joint in short axis postero-anterior (SAPA view), radionuclide bone scintigraphy and MRI scan of SI joints. All the three tests were done for both the patients and controls.

Magnetic resonance imaging scan was done using class 1.5 or 3 Tesla scanner and MRI changes of inflammation (synovial enhancement, bone marrow edema and subchondral edema) and of structural damage (erosions, sclerosis and ankylosis) were documented.[11,12]

RN scan was done using dual headed Gamma camera with SPECT-CT capabilities (SIEMENS, Symbia-T) 3 hours after standard intra venous injection of 10-20 mCi of Technitium-99m methylene diphosphate as described.[13] Due to normally increased uptake seen in the posterior views, there is misinterpretation when only qualitative analysis is used. Hence, quantitative parameters in the form of sacroiliac/sacral (SI/S) ratio were used as described elsewhere.[13] SI/S ratio in healthy controls was noted and a value that was 2 SD above this was considered abnormal and used for deciding positivity rates. This rate was compared between patients and controls. Magnetic resonance imaging positivity was considered as the gold standard against which a ROC curve was drawn with the measured SI/S ratio. The area under the curve was noted, and the sensitivity and specificity at different values documented. The presence of changes by the three

modalities was compared between patients and controls. The sensitivity, specificity and predictive values of each modality contributing to the diagnosis of SpA were assessed. All tests were considered significant at $p = 0.05$ (two-tailed). All statistical tests were done using SPSS 11.0 software.

RESULTS

A total of 42 subjects and 26 controls were included in the study and 136 SI joints analyzed (84 in patients and 52 in controls). The mean ($\pm$ SD) age of patients was 29 ($\pm$ 5.6) years and that of controls was 32.1 ($\pm$ 8.91) years (Table 1). The mean disease duration of patients was 12.5 ($\pm$ 10.2) months. Mean ESR was 33.4 in cases and 8.2 in controls. CRP was positive in 34 cases.

The plain radiograph was normal in all the patients. MRI abnormalities were present in 37/42 (88%) patients while it was uniformly normal in all the 26 controls. Out of the 37 patients with sacroiliitis on MRI, 27 (73%) had sacroiliitis on both the sides and 10 (27%) had unilateral sacroiliitis. MRI had a sensitivity of 87%, a specificity of 100%, a positive predictive value of 100% and a negative predictive value of 88.9%.

Bone marrow edema was the commonest finding inpatients with positive MRI findings.

Synovial enhancement (60%), erosions (42%), subchondral edema (46%) and sclerosis (38%) were other changes seen. The iliac aspect alone was involved in 54%, sacral aspect alone in 10%, while in the remaining 36% cases both aspects were involved.

On evaluating the RN scans, a SI/S ratio of 1.49 : 1 or more was considered abnormal. The mean ($\pm$ SD) value of this ratio in controls was 1.09 ± 0.2 and we considered $2 \pm$ SD above mean ($1.09 \pm 2 \times 0.2$) as abnormal. Considering this ratio, 34 cases were bone scan positive. Twenty-eight cases had bilateral sacroiliitis and 6 had unilateral sacroiliitis. Radionuclide bone scan had a sensitivity of 81.8% and a specificity of 87%. A Receiver Operating Characteristic (ROC) curve was drawn using SI/S ratio with the MRI abnormality as the gold standard. The area under the curve was 0.898 which was very good and the value of 1.52 had a sensitivity of 81.3% and a specificity of 90%. This corresponded quite well with $2 \pm$ SD that we had taken for our

Table 1: Characteristics and tabulated results of imaging findings in patients and controls

Characteristics	Patients	Controls	Statistics	Significance
Age (mean ± SD) in years	29 (± 5.6)	32.1 (± 8.91)	Student's t-test	Not significant
Sex (Male : Female)	34/8	21/5		
ESR	33.4	8.2	Fischer's exact test	<0.001
MRI positive	37	0		
MRI negative	5	26		
SI/S ratio on bone scan	1.50 ± 0.08	1.09 ± 0.2	Student's t-test	<0.001
SI/S ratio of mean ± 2 SD >1.49	34	0	Fischer's exact test	<0.001
SI/S ratio of mean ± 2 SD <1.49	8	26		

analysis. MRI and radionuclide bone scan abnormalities were compared in both cases and controls. None of the controls were positive with either of the modalities. The two modalities showed no significant correlation as determined by the kappa test. There were four cases who had sacroiliitis by MRI but normal bone scan and two cases had sacroiliitis by bone scan but normal MRI. Magnetic resonance imaging correlation with clinical disease activity and acute phase reactants was assessed. Both inflammatory and structural changes in MRI showed positive correlation with BASDAI (p = 0.034, 0.02 by t-test) and ESR (p = 0.02, 0.001 by t-test).

DISCUSSION

Low backache (LBA) is a common cause of disability in those less than 45 years with almost 17% of Indian population having LBA in a population-based study.[14] The prevalence of the whole group of SpAs has been recently estimated to be between 0.6 and 1.9%, with a prevalence of AS between 0.1 and 1.1%.[1]

Though only about 5 to 10% of those patients presenting with persistent LBA are likely to have SpA, it is difficult to identify an inflammatory backache from mechanical LBA. Validated criteria like Calin's for identification of inflammatory backache usually helps differentiate the two in a substantial percentage of cases.

However, imaging data, especially by conventional radiographs, were considered the 'gold standard' tool for assessing disease modification. However, radiographic progression is typically slow in AS, leading first to late detection of sacroiliitis (almost 7 to 8 years). Existence of an apt imaging modality for the purpose would go a long way in classifying a LBA patient. The 'biological' therapies have proven highly efficacious in SpAs with an acceptable safety profile. Not only did the therapy turn out to alleviate signs and symptoms but also it improved the quality of life of the patients greatly, and was shown to significantly retard the structural damage that is typical of this chronic inflammatory disorder. There is conclusive evidence for the efficacy of TNF-α blockade, both with infliximab and etanercept.[4,5]

Previous studies that attempted to evaluate the role of three imaging modalities (plain radiographs, MRI and bone scan) in early diagnosis of SpA included patients with long (up to 8 years) period of disease duration.[12,13] Magnetic resonance imaging showed maximum sensitivity (77.3%) for picking up sacroiliitis. This was closely followed by bone scan (72.7%); however, sacroiliitis was visible in only 59% of patients on plain radiographs. This study also suggested the presence of significant discordance rate between various imaging modalities. There were many limitations in these studies, one of which was the lack of controls which was addressed in the present study. For ethical reasons, controls were chosen such that they would anyway have undergone an MRI of the lumbosacral spine and SI joint due to their disease and secondly they had a proven etiology for their backache. None of the patients in our study population had evidence of sacroiliitis on conventional radiograph. This was in concordance with an earlier study in which conventional radiograph was found to be of limited utility.[15] Scintigraphy has been reported to have a high sensitivity for sacroiliitis with low specificity which is in concordance with our results also. At the traditional value of SI/S ratio of more than 1.26, RN scan had a 100% sensitivity but only 44% specificity. At a ratio of about 1.50, it had a good specificity but almost 18% patients get missed out. The bone scan was negative in all controls. Our study suggests that there is indeed a role for bone scan in screening of patient with inflammatory backache with a normal radiograph. Qualitative analysis is not enough and SI/S ratio must be done in all. A very significant advantage of the bone scan is that, it is a whole body evaluation capable of demonstrating increased activity in any of the other joints also, especially peripheral and small joints. If peripheral joints that are clinically quiescent show increased uptake, it helps in the diagnostic algorithm. As a significant addition, we have also identified that the bone scan, if done in two phases is all the more useful in assessing inflammatory activity. The two phase bone scan consists of two separate whole body images, one done 20 minutes after injection and the other one at the standard time of 3 hours post injection. This early 20 minutes image gives us a good idea of tissue and synovial hyperemia in all the joints and is usually positive in actively involved inflamed joints. As a corollary a normal bone scan has an excellent negative predictive value and rules out SpA.

Magnetic resonance imaging had an excellent sensitivity and specificity and also had excellent positive and negative predictive values and is considered the method of choice in the evaluation of sacroiliitis in patients with early SpA.[12,13] Advantages include higher quality of images, absence of ionizing radiation and capacity of detecting and differentiating acute and chronic alterations. The earliest changes can be seen by 3 months itself and not only detects structural changes but also inflammatory activity. There are few normal variants, which merit consideration during MRI evaluation of SI joint. However, MRI being a qualitative interpretation, there is a significant interobserver variation. Few of the areas of concern are, partial volume artifact between the synovial and ligamentous compartments, which can be misinterpreted as erosions. There is normally a region of high signal at the immediate subchondral marrow, on fast STIR images, which can be mistaken for early sacroiliitis. A patchy distribution of fat within the bone marrow as the sole finding should not be considered as an indicator of sacroiliitis.[16]

We found some discordance between various imaging modalities. There were two patients in whom bone scan was suggestive of sacroiliitis while MRI was normal. On further analysis of these patients it was realized that mean disease duration of the patient with positive bone scan but negative MRI was less than 4 months, probably implying that these patients would develop sacroiliitis on MRI later. Further it signifies that in the diagnosis of sacroiliitis in this group of patients, both imaging modalities may have a role. Bone scan with its high negative predictive value and sensitivity can be used for screening patients with suspected early SpA. Only the patients who are negative on bone scan may then be subsequently subjected to MRI in addition to the patients who are being considered for biologics as they may then subsequently be used for recording the response to therapy. This could be done, because, it allows for better quantitative assessment of inflammation.

The strengths of this study are the use of controls with mechanical LBA and use of quantitative analysis in RN scan. The limitations envisaged in this study include the small sample size and lack of HLA b27 data in all the patients.

CONCLUSION

Early diagnosis of SpA's is of paramount importance as there are drugs which can halt disease progression as well as give significant symptom palliation in these patients. Plain radiographs have a very limited role in early diagnosis as significant bone mineral loss has to take place before they show up and this can take up to 7 to 8 years. MRI is a highly sensitive and specific investigation and picks up inflammatory as well as structural changes of sacroiliitis and some of the changes may be apparent as early as 3 months. Bone scan, with its good sensitivity and excellent negative predictive value is another tool to picks up inflammation early. Quantitative parameter such as a raised SI/S ratio is advisable to reduce inter observer variability and false positives. An additional early tissue phase in the normal bone scan protocol is a potentially useful inflammatory index and its role needs to be elucidated in further studies. As there is some discordance between MRI and RN scan, it might be beneficial to consider these modalities as complementary where in the diagnosis is not established conclusively or where atypical presentations occur.

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