

## The usefulness of Tc-99m-MDP bone scintigraphy in detection of articular involvement of Behçet's disease

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Articular involvement was reported to be present in approximately 5–76% of Behçet patients. Therefore, we need a useful non-invasive method to detect articular involvement early in Behçet patients with nonspecific complaints. We aimed to evaluate the usefulness of <sup>99m</sup>Tc-methylene diphosphonate (Tc-99m-MDP) bone scintigraphy in the detection of the articular involvement of Behçet's disease (BD). Bone scintigraphy with Tc-99m-MDP was performed in 32 (17 male, 15 female) consecutive patients with BD. The sacroiliac (SI) joints with SI index higher than 1.34 were diagnosed as having sacroiliitis. Although joint complaints were present in only 8 (25%) patients, we detected joint involvement by scintigraphy in 27/32 (84.4%) Behçet patients mostly affecting the knees (62.5%), ankles (59.4%), SI joints (25%), wrists (21.9%), shoulders (18.7%), elbows (12.5%) and hips (3.1%). The articular involvement was monoarticular in four cases (12.5%) and was oligoarticular in the remaining. There was no correlation between joint involvement and age, gender, disease duration, drug usage or other clinical manifestations. Despite the fact that our patients were clinically asymptomatic and had normal pelvis radiography, sacroiliitis was found in 8 patients (25%). Bone scintigraphy is sensitive in the diagnosis of joint involvement allowing earlier diagnosis and showing the presence of articular involvement, especially in SI joints.

**Key words:** arthritis, Behçet's disease, bone scintigraphy, sacroiliitis

### INTRODUCTION

Behçet's disease (BD) is a chronic relapsing inflammatory disease classified among the vasculitides which may involve both arteries and veins of all sizes from different systems. Although recurrent mucocutaneous lesions may be the only symptoms in mild cases, BD is now recognized as a multisystemic disease with various organ involvements including skin, mucous membrane, eyes, joints, vessels, gastrointestinal tract and nervous system.<sup>1</sup> The joint may be the target organ in a wide variety of systemic diseases. Although arthritis has not been included in international study group criteria,<sup>2</sup> arthritis and/

or arthralgia is one of the most frequent manifestations of BD. Articular involvement was reported to be present in approximately 5–76% of Behçet patients.<sup>3–10</sup> Small and large joints and tendon enthesis can be involved in patients with BD.<sup>11</sup> Thus, we need a useful non-invasive method to detect articular involvement early in Behçet patients with nonspecific clinical complaints. To evaluate joints, <sup>99m</sup>Tc-methylene diphosphonate (Tc-99m-MDP) bone scintigraphy has not been used in Behçet patients with nonspecific arthralgia or other complaints. Several case reports have appeared on the evaluation of bone scintigraphy in patients with BD.<sup>12–14</sup>

The present study aimed to evaluate the utility of Tc-99m-MDP bone scintigraphy in the detection of the articular involvement in patients with BD. To our knowledge, no report has been published about the Tc-99m-MDP bone scintigraphy findings of BD with articular involvement.

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## MATERIALS AND METHODS

### Patients

Bone scintigraphy with Tc-99m-MDP was performed in 32 consecutive patients with BD. The diagnostic criteria of the International Study Group of Behçet's disease were used for the diagnosis.<sup>2</sup> The clinical manifestations of the patients were recorded and routine laboratory tests were performed. To evaluate articular involvement, X-ray examinations were performed. In laboratory investigations, erythrocyte sedimentation rate (ESR), leucocyte count, C-reactive protein (CRP), and rheumatoid factor (RF) were investigated. Eighteen patients were on 1.5 mg/day colchicine treatment only, 5 patients were on colchicine plus prednisolone (5–15 mg/day), 4 patients were on colchicine plus azathioprine (2 mg/kg/day), one patient was on colchicine plus sulphasalazine (1.5 g/day) and 4 patients were without treatment.

### Bone scintigraphy

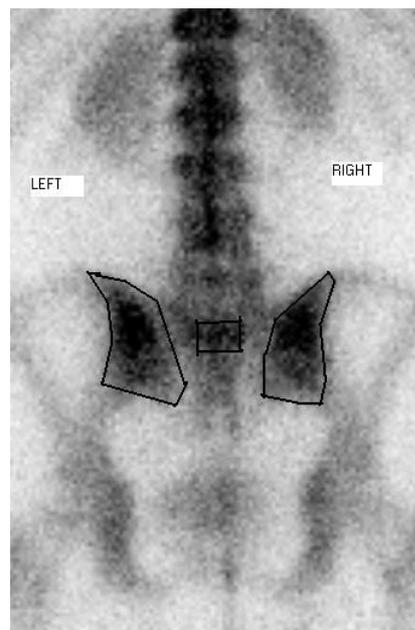
After informed consent was obtained from all patients, three-phase sacroiliac (SI) joint and whole body bone scintigraphies were performed after intravenous injection of 555–740 MBq (15–20 mCi) of Tc-99m-MDP using the gamma camera (Siemens E-Cam Variable) with a double head detector equipped with a low-energy, high-resolution collimator. After obtaining whole body images, pelvis and spot images of both upper and lower extremity joints were also obtained. Two experienced physicians evaluated the images obtained. The SI index was calculated as the ratio between the total number of counts in the region of interest placed on the SI joints and an identical region placed on the sacrum on the posterior pelvis images. The SI joints of patients with an SI index that was higher than 1.34 were diagnosed as having sacroiliitis<sup>15,16</sup> (Fig. 1).

### Statistical analysis

Data were analyzed using the statistical package SPSS for Windows (Ref. 9.05, SPSS Inc., Chigago, IL, USA). Results were expressed as mean  $\pm$  SD. Statistical significance was set at the 0.05 level. Pearson correlation analysis was performed for correlation of both arthritis with age, disease duration, clinical and laboratory features and drug usage.

## RESULTS

Of the 32 Behçet patients, 17 (53.1%) were male and 15 (46.9%) were female with a mean age of  $40.94 \pm 12.05$  yr. Demographic characteristics and some laboratory findings of patients were shown in Table 1. Among clinical manifestations, oral aphthous lesions (n = 32, 100%), genital ulcers (n = 18, 56.2%), ocular lesions (n = 7, 21.8%), cutaneous lesions including papulopustular and/or acneiform lesions and/or erythema nodosum (n = 14, 43.7%)



**Fig. 1** Sacroiliac and sacral ROIs used in determination of SI index. (ROIs: Region of Interest, SI: Sacroiliac)

**Table 1** Demographic characteristics and laboratory findings of the patients (mean  $\pm$  SD)

Number of patients	32
Gender (M : F)	17 : 15
Mean age (year)	$40.94 \pm 12.05$
Disease duration (months)	$123.06 \pm 88.24$
CRP	$11.868 \pm 25.64$
ESR	$16.75 \pm 13.15$

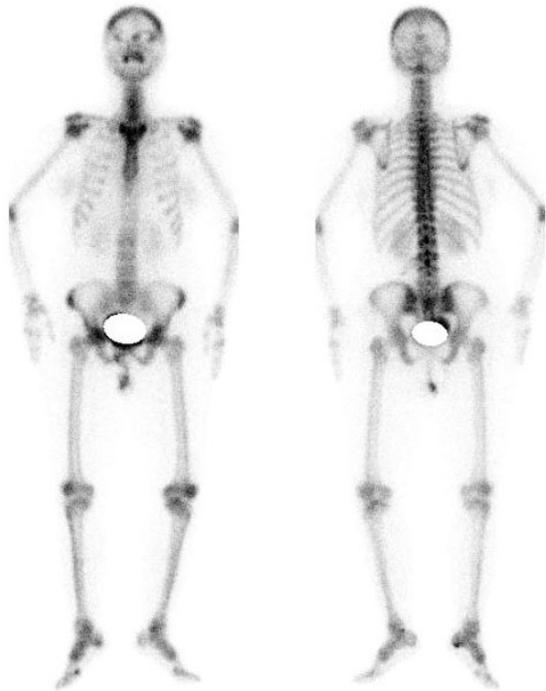
CRP: C-reactive protein, ESR: erythrocyte sedimentation rate

**Table 2** Joint involvement in patients with Behçet's disease

	Number of patients	Percent
Knee	20	62.5
Ankle	19	59.4
Sacroiliac*	8	25
Wrist	7	21.8
Shoulder	6	18.7
Elbow	4	12.5
Hip	1	3.1

\*The patients with sacroiliac (SI) index higher than 1.34 were diagnosed with sacroiliitis.

were found. One patient (3.1%) had vascular involvement (deep vein thrombosis, confirmed by clinical findings and Doppler ultrasonography), although three patients (9.3%) had gastrointestinal involvement, and eight patients (25%) had articular involvement (6 patients had arthralgia, 2 patients had oligoarthritis during the enrollment). None of the patients had cardiac or neurologic involvement. RF was negative in all patients.



**Fig. 2** Images of multiple joint involvement in one case. Whole-body image shows increased activity in multiple joints such as bilateral shoulder, bilateral knee, right ankle, bilateral hip and bilateral sacroiliac joints.

Tc-99m-MDP bone scintigraphy demonstrated articular involvement in various joint regions. Joint involvement was found in 27 (84.4%) of patients by bone scintigraphy. Four patients (12.5%) had monoarticular, and the others had oligoarticular involvement. The regions of joint involvement of our patients were shown in Table 2. Sacroiliac joint involvement was found in 8 of patients with BD. Four of them were bilateral. These patients were clinically asymptomatic and had normal pelvic radiography. Images of a patient with multiple joint involvement are shown in Figure 2.

There was no further correlation between type of articular involvement and age, disease duration, treatment modality or other clinical manifestations. In addition, there was no correlation between SI index and age as well as disease duration, treatment modality or other clinical manifestations.

## DISCUSSION

Since the original description, multiple systemic associations of the BD have been recognized including articular, vascular, gastrointestinal, cardiopulmonary and neurological involvement.<sup>1</sup> Arthritis has been found at the time of diagnosis in Behçet patients, and 9% of patients have arthritis only as an initial manifestation.<sup>9,17</sup> In BD, joint symptoms have usually been described as intermittent, self-limiting, non-erosive, mostly monoarticular and

oligoarticular arthritis.<sup>9,17,18</sup> Oligoarthritis can also be found in small and large joints.<sup>4-6,9</sup> The most frequent sites of involvement are knees, ankles, wrists, and elbows.<sup>6,9,11,18,19</sup> Also, involvement of SI and spinal joints has been reported.<sup>5</sup> Back pain due to sacroiliitis in patients with BD may occur.<sup>20</sup> The involvement of SI joint in patients with BD is different than that of reactive arthritis because the involvement is unilateral.<sup>3</sup>

Although joint manifestations have become a well-known part of the spectrum of multisystemic involvement in BD, previous reports have been limited to conventional radiographic findings. Findings have been described as being normal or showing mild abnormalities consisting of nonspecific findings such as osteoporosis, soft-tissue swelling with joint-space narrowing, osteophyte formation and marginal erosions, rarely.<sup>19,20</sup> Therefore, it was reported that quantitative bone scintigraphy could be an important objective test for evaluating joint involvement in BD as an inflammatory disease.<sup>23,24</sup> Bone scintigraphy with Tc-99m-MDP has been widely used for imaging of arthritis. High bone turnover taking place in the inflamed joints leads to a high uptake of Tc-99m-MDP, which also concentrates in areas of increased vascularity.<sup>25</sup> In synovitis there is an increased periarticular uptake of technetium diphosphonate because of the anastomotic vessels coming to bone from the inflamed synovium.<sup>26</sup> In addition, increased bone activity in the SI joints was shown to be a sensitive diagnostic method in sacroiliitis.<sup>24</sup> We recently evaluated joint involvement in familial Mediterranean fever (FMF) patients with or without joint symptoms by Tc-99m-MDP bone scintigraphy and found that arthritis was present in 72% of patients with sacroiliitis found in 50%, who were mostly asymptomatic.<sup>27</sup> Despite the fact that joint complaints were found clinically in 8 (25%) patients, we detected joint involvement in 27/32 (84.4%) of patients with BD. Knees (62.5%) and ankles (59.4%) were found to be the most affected extremities. Involvement of the sacroiliac joints, wrists, shoulders and elbows was also found in decreasing percentages. In our study, involvement of large joints was most common. There was no correlation between joint involvement and age as well as gender, disease duration, drug usage or other clinical findings. In our Behçet patients, clinically, joint involvement was observed with a relatively lower frequency as compared to previous reports.<sup>3,4,10</sup> However, our results were similar to those regarding other Turkish patients.<sup>18,28</sup> In our patients, joint involvement such as that of knee, ankle, elbow, wrist and shoulder was slightly higher than in previous studies.<sup>9,10</sup>

Despite the fact that our Behçet patients were clinically symptom-free and had normal pelvis radiography, sacroiliitis was found in 8 patients (25%). Four of them had bilateral sacroiliitis. The development of sacroiliitis in BD is still controversial. Some investigators have reported a high prevalence of sacroiliitis in BD and suggested that BD should be included in seronegative

spondyloarthropathy complex, whereas recent reports suggest no association between the two conditions.<sup>23,29–31</sup> These discordant results might be due to a high observer variation in interpreting the film of anteroposterior view of the pelvis. Magraoui et al.<sup>32</sup> reported SI joint involvement in Behçet's disease in 7.4% of cases by using X-ray and computed tomography (CT), and the frequency of sacroiliitis in the BD group was slightly increased without statistical significance when compared to healthy controls. In the current study, the frequency of sacroiliitis was much higher than in the previous studies.<sup>32,33</sup> The involvement of SI joints in patients with BD was usually evaluated in association with clinical examination and by plain radiography or CT. We believe that this difference could be explained by the use of different methodology for screening of joints. In fact, the SI joint is perhaps the most difficult one in the body to image, because of its complex anatomy and undulating articular surfaces. Since bone scintigraphy is more sensitive in the diagnosis of joint involvement than clinical examination or conventional radiological imaging methods, it facilitates detection of joint involvement even in the asymptomatic phase and shows the presence of inflammation in multiple sites. Miron et al.<sup>34</sup> suggested that it might be useful even before the appearance of radiological abnormalities. In addition, it was proposed as a sensitive method for the diagnosis of early sacroiliitis.<sup>35,36</sup> The reason why higher ratios are not found in our study is that our patients had relatively longer disease duration and were on anti-inflammatory treatment during our investigation. Indeed, it was reported that anti-inflammatory treatment could lead to decreased uptake ratios in SI joint.<sup>37</sup>

In conclusion, BD is often associated with articular involvement. These patients may have mild symptoms or be asymptomatic and also have normal plain radiographic findings. However, the joint involvement should be detected using bone scintigraphy. This is a noninvasive test and an alternative method to detect joint involvement especially in the early stage of the disease. Therefore, we suggest that bone scintigraphy can be used in patients with BD to determine the presence of articular involvement especially in SI joints even in asymptomatic cases.

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