

TC-99m-MDP Bone Scintigraphy Utilization for Articular Involvement Detection among Behçet's Patients

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ABSTRACT

Background: Behçet's disease (BD) is characterized by inflammation of the arterial and venous walls throughout the body and has an unknown cause.

Objective: This study was aimed to assess articular involvement in patients with Behçet's disease: a pilot study with bone scintigraphy.

Patients and Methods: This study included a total of 25 Behçet's disease patients, attending at Departments of Radiodiagnostics and Nuclear Medicine, Cairo University Hospitals. They were subjected to the following: Full history taking, clinical examination, routine laboratory tests including CBC, ESR, CRP and conventional radiological examination and bone scintigraphy in the radiodiagnosis and the nuclear medicine departments respectively, Cairo University Hospital. Skin pathergy test was performed.

Results: Joint involvement was clinically apparent in 12 of the 25 cases (48%). Two individuals (8 percent) had signs of rheumatoid arthritis in their hands. The most frequently involved site on bone scintigraphy was the wrist (100%). All of the patients (100%) revealed hand scintigraphic involvement, 24% of them had mild score, 60% had moderate score and 16% had severe score.

Conclusion: It could be concluded that bone scintigraphy is helpful in identifying articular involvement and pinpointing its location.

Keywords: Behçet's disease, TC-99m-MDP Bone Scintigraphy Utilization, Articular Involvement.

INTRODUCTION

Veins and arteries of varying sizes can be affected by Behçet's disease (BD), a chronic inflammatory condition of unknown origin. The skin, mucous membrane, eyes, joints, arteries, digestive system, and neurological system are only some of the organs that might be affected by Behçet's disease ⁽¹⁾.

Nevertheless, arthritis is not among the criteria used in international studies ⁽²⁾, Behçet's disease is characterized by a variety of symptoms, one of the most common of which being arthritis or arthralgia. In the range of 5-76 percent of Behçet patients, articular involvement was identified. Behçet's disease affects both small and large joints, as well as the tendon enthesis ⁽³⁾.

⁹⁹ mTc-methylene diphosphonate (TC-99m-MDP) bone scintigraphy is a non-invasive method for detecting early subclinical articular involvement in Behçet patients ⁽⁴⁾. Bone scintigraphy has a high sensitivity for detecting joint involvement in its earliest stages, especially in asymptomatic or mildly symptomatic patients whose plain radiographs look normal ⁽⁵⁾.

This study was aimed to assess articular involvement in patients with Behçet's disease: a pilot study with bone scintigraphy.

SUBJECTS AND METHODS

This study included a total of 25 Behçet's disease patients, attending at Departments of Radiodiagnostics and Nuclear Medicine, Cairo University Hospitals. Patients were subjected to the following: Comprehensive medical history, physical examination, standard laboratory testing (complete blood count, electrolytes, C-reactive protein), and conventional

radiographic examination and bone scintigraphy. A test for skin allergies was conducted.

Pathergy test:

Each individual had a pathergy test (in which 0.2 ml of saline was injected intradermally into an avascular area of the flexor aspect of the forearm). If a sterile papule appears within 24 to 48 hours, the test is considered positive (simple erythema was accepted as negative). For further confirmation of the diagnosis, one of the dermatology department's employees consulted with a dermatologist.

The severity score was arrived at by adding together the points given for each symptom, with one point given for mild symptoms, two for moderate symptoms, and three for severe illness presentations ⁽⁶⁾.

Bone Scintigraphy using Tc-99m MDP:

• Preparation and follow-up with patients:

- The patient should not be in a fasting state.
- The patient is instructed to take about 500-1000 ml (0.5-1L) of water or other drink types over a period of 2-3 hours and void regularly as no need to retain urine in urinary bladder.
- Both before and after an imaging session, the patient should empty his or her bladder often (reduces radiation dose to the bladder wall).
- Prior to imaging, the patient should empty their pockets of any metal (jewellery, money, keys, etc.).

• **Dose:** 15-20 mCi (555-740 MBq) Tc-99m-MDP (adult dose).

- **Mode of administration:** Intravenous injection.
- **Imaging:** Between two and four hours after injecting the tracer.
- **Procedure:**
 - A total body scan that takes between 15 and 20 minutes and provides an anterior and posterior picture of the bones.
 - You should aim for 300k - 500k counts per image for the wrist spot view.
 - Using a low-energy, high-resolution collimator, and a gamma camera [Philips Marconi (axis) with twin head detector].

• **Post- imaging precautions:**

The patient is instructed to continue for soft drinks uptake, voiding the urinary bladder and avoid close contact with pediatric age group and pregnant females for 4 half life of the used tracer (Tc-99m-MDP) i.e. 4×6 HRS=24HRS (7).

Ethical consent:

The study was authorized by Cairo University's Ethical Institutional Review Board. All study participants provided written informed permission after being informed of our research's goals. The Declaration of Helsinki for human beings, which is the international medical association's code of ethics, was followed during the conduct of this study.

Statistical analysis

In order to analyze the data acquired, Statistical Package of Social Services version 28 was used to execute it on a computer (SPSS). In order to convey the findings, tables and graphs were employed.

The quantitative data was presented in the form of the mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t test (T) is used to assess the data while dealing with quantitative independent variables. Pearson Chi-Square and Chi-Square for Linear Trend (X2) were used to assess qualitatively independent data. The significance of a P value of 0.05 or less was determined.

RESULTS

This study included 25 patients with BD. Their average age was (32.44±7.78) ranged from 20 to 44 years. Eighteen patients were males (72%) and seven patients were females (28%). To determine how long someone had BD, researchers counted the number of years between when their initial BD symptoms appeared and when their sample was taken. The time frame might be anywhere between 9 months and 16 years with a mean of 6.98±4.61 years (Table 1).

Table (1): Characters BD patients.

Patients (n=25)	Mean±SD	Range
Age	32.44±7.78	20 years-44 years
Disease Duration	6.98±4.61	9 months-16 years
Gender		
Male:	18 (72%)	
Female:	7 (28%)	

Conventional radiological examination and bone scintigraphic evaluation of the hands of BD patients were found to have positive correlation with the age and disease duration, though without statistical significance (Table 2).

Table (2): Comparison of BD patients' ages and disease durations with the results of hand x-rays and hand bone scans.

Item	Hand X-rays	Hand bone scan
Age		
r	0.229	0.295
P	0.501	0.666
Significance	NS	NS
Disease duration		
r	0.114	0.308
P	0.848	0.622
Significance	NS	NS

Comparative study between the three groups of patients according to their hand bone scan score as regards their clinical features revealed non-significant differences (Table 3).

Thirteen of patients (n=25) who had no joint manifestations either arthralgia or arthritis were found to have hand x-rays findings in the form of: 7 patients (out of 13 patients) had juxta-articular osteopenia, and 2 patients (out of 13 patients) had juxta-articular osteopenia and narrowing PIPs joint spaces.

They were found to have hand bone scan involvement in the form of moderate severity score. Only one of our patients had CNS manifestations in the form of right hemiparesis, she had hand x-ray involvement in the form of juxta-articular osteopenia and mild narrowing in PIP joint spaces and she had moderate severity score in hand bone scan. Three of our patients had EN; all of them had hand x-ray involvement in the form of: 1 patient had juxta-articular osteopenia and mild narrowing in PIP joint spaces, 1 patient had juxta-articular osteopenia only and the other one had juxta-articular osteopenia and reduced intercarpal bone spaces and their hand bone scan revealed mild severity score in two patients and severe score in one patient (Table 3).

Table (3): Comparison between the 4 point scales of hand bone scintigraphy as regard clinical manifestations.

Item	Hand bone scintigraphy score			P	Sig
	Mild	Moderate	Severe		
Oral ulcers: Present 14 Absent 11	4 2	8 7	2 2	0.827	NS
Genital ulcers: Present 5 Absent 20	2 4	3 12	0 4	0.435	NS
Arthralgia& or arthritis: Present 12 Absent 13	3 3	6 9	3 1	0.569	NS
Uveitis: Present 11 Absent 14	2 4	8 7	1 3	0.496	NS
Major vessel: Present 8 Absent 17	2 4	5 10	1 3	0.948	NS
Pathergy: Present 4 Absent 21	1 5	2 13	1 3	0.851	NS
Acne: Present 3 Absent 22	1 5	1 14	1 3	0.558	NS
EN: Present 3 Absent 22	2 4	0 15	1 3	0.072	NS
CNS: Present 1 Absent 24	0 6	1 14	0 4	0.707	NS

According to the sex distribution in our BD patients, we compared between both groups as regard clinical joint involvement, hand x-ray and hand bone scan findings (Table 4). We found higher incidence of joints involvement (clinical and radiological) in female group than male, though with no statistical significance.

Table (4): Comparison between male and female groups as regards clinical joint involvement, hand x-ray and hand bone scan findings.

Item	Male(n=18 pt)	Female(n=7 pt)	P	Sig
•Arthralgia& or arthritis: Present 12 Absent 13	8 (44.5%) 10(55.5%)	4 (57.1%) 3 (42.9%)	0.569	NS
•Hand x-ray involvement: Present Absent	13(72.2%) 5 (27.8%)	6 (85.7%) 1 (14.3%)	0.479	NS
•Hand bone scan: Mild Moderate Severe	5 (27.8%) 11(61.1%) 2 (11.1%)	1 (14.3%) 4 (57.1%) 2 (28.6%)	0.508	NS

According to the ESR value (1st hour), we compared between patients with ESR ≤20 mm/hr and those with ESR >20 mm/hr as regard clinical joint involvement, hand x-ray and hand bone scan findings. We found significant difference between both groups in the hand bone scan results (higher incidence of abnormal bone scan especially of moderate severity score was observed in the group of higher ESR). According to the presence or absence of CRP, we didn't find any significant difference between patients with +ve CRP and those with -ve CRP as regard the clinical joint involvement, radiological and bone scan findings, though patients with +ve CRP had slightly higher incidence of clinical and radiological involvement, and most of them showed moderate severity score on hand bone scan (Table 5).

Table (5): Comparison between patients with ESR ≤ 20 mm/hr and those with ESR > 20 mm/hr, ve CRP and those with -ve CRP as regard clinical joint involvement, hand x-ray and hand bone scan findings.

Item	Normal ESR (≤ 20 mm/hr) (n=12 pt)	High ESR (>20 mm/hr) (n=13 pt)	P	Sig
•Arthralgia &or arthritis: Present Absent	8 (66.7%) 4 (33.3%)	4 (30.8%) 9 (69.2%)	0.073	NS
•Hand x-ray involvement: Present Absent	9 (75%) 3 (25%)	10 (76.9%) 3 (23.1%)	0.091	NS
•Hand bone scan: Mild Moderate Severe	5(41.7%) 4(33.3%) 3(25%)	1 (7.7%) 11(84.6%) 1 (7.7%)	0.03	Sig
	+ve CRP (n=12 pt)	-ve CRP (n=13 pt)	P	Sig
•Arthralgia &or arthritis: Present Absent	6 (50%) 6 (50%)	6 (46.2%) 7 (53.8%)	0.84	NS
•Hand x-ray involvement: Present Absent	10(83.3%) 2 (16.7%)	9 (69.2%) 4 (30.8%)	0.41	NS
•Hand bone scan: Mild Moderate Severe	2 (16.7%) 9 (75%) 1 (8.3%)	4 (30.8%) 6 (46.2%) 3 (23%)	0.32	NS

According to disease activity score, no significant difference was found between active and inactive groups as regard the clinical joint involvement, radiological and bone scan findings; however there was a slightly higher incidence of clinical joint involvement in active group (Table 6).

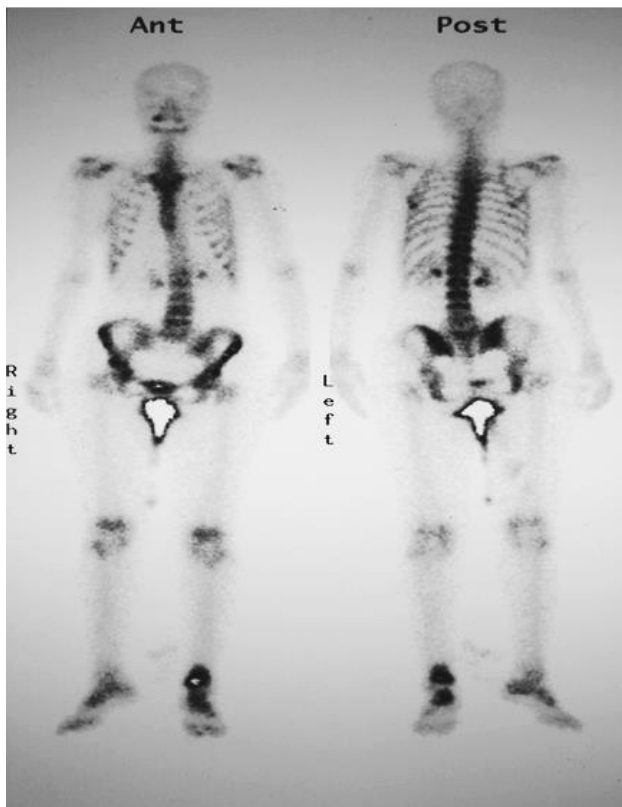
Table (6): Comparison between the active and inactive groups of patients as regard clinical joint involvement, hand X-ray and hand bone scan findings.

Item	Active group (n=14pt)	Inactive group (n=11pt)	P	Sig
•Arthralgia &or arthritis: Present Absent	8(57.1%) 6(42.9%)	4(36.4%) 7(63.6%)	0.30	NS
•Hand x-ray involvement: Present Absent	11(78%) 3(21%)	8(72%) 3(27%)	0.734	NS
•Hand bone scan: Mild Moderate Severe	5(35%) 7(50%) 2(14%)	1(9%) 8(72%) 2(18%)	0.300	NS

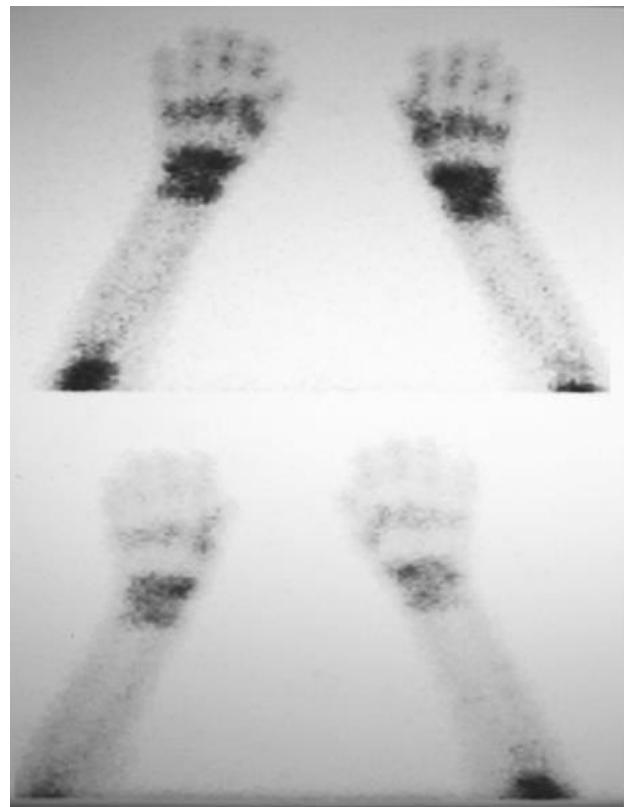
Table (7) showed slight increase in the clinical and radiological findings among the patients with high disease severity score, though with no statistical significance.

Table (7): Comparison between patients disease severity score as regard the clinical joint involvement, hand x- ray and hand bone scan findings:

Item	Group I (No=17)	Group II (No=8)	P	Sig
•Arthralgia &or arthritis: Present			0.06	NS
Absent	6 (35%)	6 (75%)		
•Hand x-ray involvement: Present	11 (65%)	2 (25%)	0.624	NS
Absent	5 (29%)	7 (87.5%)		
•Hand bone scan: Mild	12 (70.5%)	1 (12.5)	0.958	NS
Moderate	4 (23%)	2 (25%)		
Severe	9 (52%)	6 (75%)		
	4 (23%)	0 (0%)		



(A) Bone scan image of whole body showed increased uptake in left ankle and left sacroiliac joints



(B) Bone scan image shows increased uptake in multiple joints such as bilateral wrists, bilateral MCPs and bilateral PIPs joints



(C) Plain x-ray of hands shows juxta-articular osteopenia and mild narrowing in PIPs joint spaces



(D) Plain x-ray of sacroiliac joints show narrowed right SIJ space and sclerosis

Figure (1): female patient aged 25 years with no clinical joint involvement, her bone scan and x-ray findings showed in figures A, b, C, and D.

DISCUSSION

Variations in patient clinical characteristics and frequencies of organ involvement have been found across studies of BD patients from different regions (such as Turkey, North of Africa, Egypt, Tunisia, Morocco), and East of Asia (China, Japan, and Korea), suggesting that geographic, environmental, and genetic factors likely play a role in the pathogenesis of the disease and its sequelae⁽⁸⁾.

Our study involved 25 BD patients with a mean age of 32.44±7.78 years and mean disease duration of 6.98±4.61 years. Such age presentation was comparable with the age reported by other studies as **Nam et al.**⁽⁹⁾, **El-Maghraoui et al.**⁽¹⁰⁾ and **Alekberova et al.**⁽¹¹⁾.

In the current study, the incidence of disease was more common in males than females (♂: ♀ ratio was 2.1:1); in agreement with the studies conducted in Middle Eastern countries⁽¹²⁾. On the contrary, there was a female predominance in studies from Brazil⁽¹³⁾.

Oral and genital ulcers were found in 56% & 20% of our patients respectively compared to 100% & 55% in **Chen and Chang**⁽¹⁴⁾ study and 93% & 75.4% in **Yurtkuran et al.**⁽⁷⁾ study.

Regarding the skin lesion and positive supportive periodontal therapy (SPT) we have found 24% & 16% positivity respectively compared to an incidence of 16% positivity in Morocco carried out study⁽¹⁰⁾, and we can notice the agreement with that North African study. However, this was not the case with the Tunisian study done by **Hamzaoui et al.**⁽¹⁵⁾ as he reported positive SPT of 51%. However, **Yurtkuran et al.**⁽⁷⁾ reported a higher incidence of positive SPT that reached 61.4%.

Our study agreed in the percentage of eye manifestation (44%) with **Hamzaoui et al.**⁽¹⁵⁾ carried out on Tunisian BD patients and found 32.2% of eye involvement.

According to **Alan et al.**⁽¹⁶⁾, Behçet's illness was characterized by atypical fibro musculoskeletal manifestations, and in 25% of patients, vascular involvement is possible. Based on the results of our investigation, we determined that it was around (32 percent). However, a higher value of (50%) was given by **Tănăseanu et al.**⁽¹⁷⁾. **El-Maghraoui et al.**⁽¹⁰⁾ and **Houman et al.**⁽¹⁸⁾ reported 33% of vascular involvement, in agreement to our study. While **Sahin et al.**⁽¹⁹⁾ recorded only 3.1%. So we got a variable range from 3-50% and some keeps with us and other disagrees and we believe this is due to difference may be in study design or age group or racial and environmental factors.

Only 4% of our patients presented with arthritis as their initial symptom. This rate was significantly lower than that reported by **Ait Badi et al.**⁽²⁰⁾, who examined 79 Moroccan patients and found an incidence of 16.5%.and then that (9%) reported by **Sahin et al.**⁽¹⁹⁾. A 10.9% was reported by **Alekberova et al.**⁽¹¹⁾.

In the present study, among patients with joint involvement, 75% was manifested by arthralgia, and 25% by arthritis with or without arthralgia. It was oligoarticular in 58.4% of patients, monoarticular in

33.3%, and polyarticular in 8.3%; symmetrically distributed, and mostly affecting the knee and hand joints. **Park et al.**⁽²¹⁾ reported that knee, proximal interphalangeal and metacarpophalangeal joints were the main sites. **Nam & Kim**⁽⁹⁾ According to the data, knees (68%), proximal interphalangeal joints (33%), wrists (27%), and ankles (24%) were the most often affected joints. Among the patients, oligoarticular involvement was seen in 18 (55 percent), polyarticular in 9 (27 percent), and monoarticular in 6 (10 percent) (18 percent). **Cheng et al.**⁽²²⁾ reported oligoarthritis in 73.3% of BD patients with joint disease. **Gur et al.**⁽²³⁾ revealed that asymmetric oligoarthritis was the most prevalent kind, occurring in 65.3% of patients, and that the wrist (53.8%) and knee (27% of patients) were the most common sites of involvement (50 percent). **Ait Badi et al.**⁽²⁰⁾ reported that inflammatory arthralgias were the most common manifestation and observed in 81%, involved mainly the large lower limb joints. **Yang et al.**⁽²⁴⁾ found that the most common involved site was the knee joint (60 of 87 cases), and multiple site involvement was common (56.0%).

When we correlated hand x-ray and hand bone scintigraphic findings with the age and the disease duration we found a positive correlation but with no statistical significance. However, this was not in agreement with **Yurtkuran et al.**⁽⁷⁾ whose hand scintigraphy was shown to have a statistically significant relationship to illness duration but no relationship to patient age, as was the case in our investigation. Possible causes of this discrepancy include the prolonged illness duration of their patients (2–35 years vs. 9–16 years in our patients). As was already established, their research was conducted on the hands of people with BD. But our findings are in agreement with **Sahin et al.**⁽¹⁹⁾ study as they reported non-significant correlation between articular involvement detected by bone scintigraphy with age and disease duration.

Our study found nonsignificant correlation between hand bone scintigraphic findings and the different disease manifestations such as oral ulcers, genital ulcers, eye lesions, skin lesions, arthritis, vascular, neurological involvement and pathergy test. These results are in agreement with the results of **Yurtkuran et al.**⁽⁷⁾ who also reported no significant correlation between specific organ involvement and hand scintigraphic involvement. In addition, **Sahin et al.**⁽¹⁹⁾ were unable to find correlation between scintigraphic articular involvement and other clinical manifestations. We found slightly higher incidence of joints involvement (clinical and radiological) in female group, though with no statistical significance. **Yurtkuran et al.**⁽⁷⁾ revealed a statistically insignificant increase in the proportion of female patients among those with hand scintigraphic involvement.

Our study found significant correlation between hand bone scintigraphic findings and ESR, but not with CRP. **Yurdakul et al.**⁽²⁵⁾ shown that the ESR was

significantly but only marginally increased during exacerbations compared to quiescent times in people with arthritis, and that the ESR was significantly higher in those with arthritis than in patients without joint involvement. We may infer that both ESR and CRP have limited utility in monitoring the arthritis of BD due to the illness's diverse nature of organ involvement, its fluctuating history, and the absence of dependable laboratory indicators suitable for reflecting overall disease activity.

In our study, no significant difference was found between scintigraphic hand involvement and clinical activity or severity disease scores, in agreement with **Yurtkuran et al.** (7) who couldn't confirm whether hand scintigraphic findings were indicators of disease activity or prognosis.

CONCLUSION

One might get the conclusion that bone scintigraphy is helpful in identifying articular involvement and pinpointing its location. When a patient with subclinical arthritis comes under our care, we keep a close eye on them to make sure they don't progress to full-blown arthritic.

To confirm the present results and show the prevalence of articular involvement in Egyptian BD patients, it is recommended to conduct follow-up for patients with subclinical arthritis to identify the development of frank arthritis, and to conduct additional research on a larger number of patients.

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