Cardiac and skeletal muscle scintigraphy in dermato- and polymyositis: clinical implications

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Abstract. To determine the role of scintigraphy in the detection of skeletal and cardiac involvement in dermato- and polymyositis (DM/PM), we studied 30 patients with a confirmed diagnosis of DM/PM (23 females, 7 males; mean age: 35 years). Technetium-99m pyrophosphate (^{99m}Tc-PYP) and gallium-67 scans showed similar sensitivity, specificity and accuracy in the detection of skeletal muscle involvement when compared with serum enzymes (70%, 100% and 80%, respectively). Compared with the clinical parameters, ^{99m}Tc-PYP showed 70% and ^{67}Ga 65% accuracy. Abnormal PYP cardiac uptake was observed in 57% of patients, whereas abnormal ^{67}Ga cardiac uptake was seen in only 15%. Electrocardiography was abnormal in 40%, rest gated blood pool study in 23%, and chest X-ray in 13%. In conclusion, both ^{99m}Tc-PYP and ^{67}Ga can be useful in the detection of the active phase of muscle disease. However, ^{99m}Tc-PYP seems to be more effective than ^{67}Ga in the early diagnosis of cardiac involvement.

Key words: Polymyositis/dermatomyositis – Cardiac imaging – Technetium-99m pyrophosphate – Musculoskeletal imaging – Gallium-67 – Gated blood pool

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Introduction

Polymyositis (PM) is a treatable inflammatory myopathy of unknown aetiology, clinically characterized by thoracic and pelvic girdle weakness. Dermatomyositis (DM) is considered to be present when typical cutaneous lesions (Gottron and heliotrope) are also observed. Although the striated muscle is the target organ, it is not uncommon to detect systemic involvement with pulmonary, digestive and cardiac complications.

The disease is usually well controlled upon oral administration of corticosteroids. However, long-term corticosteroid therapy may produce some side-effects which force unexpected withdrawal or modifications in the therapeutic approach.

Since the muscle weakness is the major source of morbidity in DM/PM, it is crucial to conduct an effective follow-up in order to prevent permanent disability. The quantitative evaluation of muscle strength is one of the most valuable tests for monitoring the inflammatory activity. However, its subjectivity and lack of correlation with other parameters have been widely reported [1]. The serum levels of muscle enzymes, such as creatine phosphokinase (CPK), aldolase, and lactate dehydrogenase (LDH), have been extensively used. However, while this is a low-cost method with high availability, false-negative results have been reported [2]. It is not uncommon to see a clinical-laboratory discordance. In such circumstances it is difficult for clinicians to determine whether to interrupt or to maintain the corticosteroid therapy. Therefore, a search for more effective techniques to monitor the inflammatory activity is necessary.

Cardiac involvement, although first noted by Oppenheim in the nineteenth century [3], is seldom diagnosed by clinical examination. Controversies still exist about its incidence, natural history and even prognostic implications. A non-invasive procedure capable of detecting early cardiac involvement and dysfunction would be helpful in the management of these patients.

The aims of this study were (1) to evaluate the sensitivity, specificity and accuracy of scintigraphy in the detection of skeletal muscle involvement when compared to enzymatic and clinical parameters, and (2) to determine the frequency of cardiac involvement in polymyositis through scintigraphic evaluation.

Materials and methods

Thirty patients (pts) with documented PM/DM (23 women, 7 men; 8–59 years) were sequentially studied. All of them were at different stages of the disease, but while in the acute phase they all met the diagnostic criteria proposed by Bohan and Peter [4], which include: (1) muscle weakness, (2) elevation of serum levels of muscle enzymes, (3) myopathic pattern on electromyography,

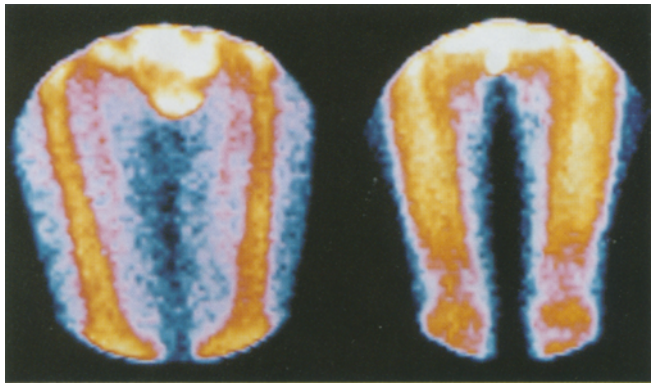

Fig. 1. Example of a normal scan (*left*) and marked ^{99m}Tc-pyrophosphate accumulation in skeletal muscles of the thigh (*right*)

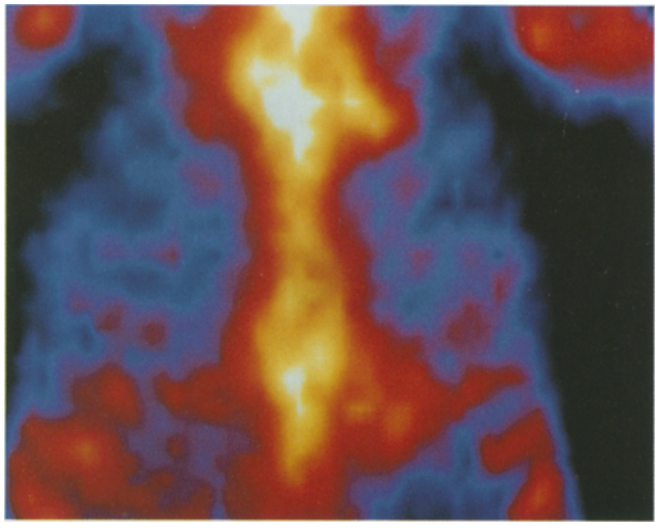

Fig. 2. ^{99m}Tc-pyrophosphate myocardial scan. Anterior projection of the chest. Example of a patient with a score of 2+

(4) typical histological changes of myositis and (5) typical skin lesions.

Nineteen patients fulfilled the Bohan and Peter criteria for definite PM/DM and 11 the criteria for probable disease. No patient with criteria for possible disease was included in this trial.

According to the classification proposed by Bohan and Peter, the patients were divided into five different categories as follows: I=polymyositis (8 pts), II=dermatomyositis (14 pts), III=myositis associated with malignancy (2 pts), IV=childhood dermatomyositis (4 pts) and V=overlap syndrome (2 pts).

Muscle strength was assessed according to the method of the British Medical Research Council (BMRC). Grades from 0 (no muscle strength) to 5 (normal muscle strength) were assigned in order to permit comparison with the other parameters of muscle inflammatory activity [5]. Scores below 4 were considered an indication of active disease. Laboratory evaluation consisted of measurement of CPK, LDH and serum glutamic-oxaloacetic transaminase (SGOT). All enzymes were measured using a kinetic UV test in a Cobas Mira Plus instrument.

Cardiac evaluation consisted of standard chest X-ray and electrocardiography (ECG). All patients underwent ^{99m}Tc-pyrophosphate scan (^{99m}Tc-PYP) and gated blood pool imaging. Imaging was begun 6 h after the intravenous injection of 8 MBq/kg of ^{99m}Tc-PYP. Images with a minimum of 500 k counts were obtained with a conventional scintillation camera equipped with a low-energy high-resolution collimator. In addition to ^{99m}Tc-PYP

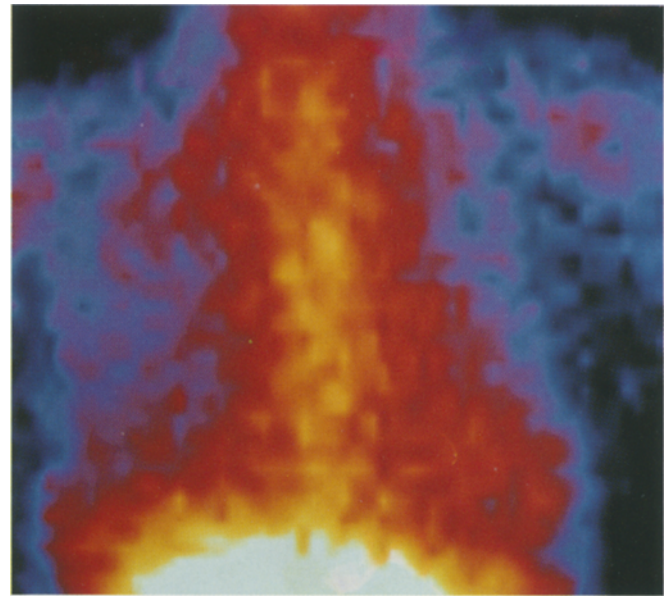

Fig. 3. ^{67}Ga myocardial scan. Anterior projection of the chest showing mild uptake of ^{67}Ga in the heart. This patient had no symptoms and minor ECG abnormalities

scan, 20 patients were also investigated with gallium-67. The images were obtained 48 h after an intravenous injection of 1.6 MBq/kg of ^{67}Ga, using a medium-energy collimator. Peripheral muscle imaging consisted of anterior and posterior projections of the entire body for both studies. Myocardial images were obtained in the anterior, left anterior oblique 45° (LAO 45) and left lateral projections of the chest. Equilibrium gated blood pool imaging with 16 frames/R-R interval was initiated 15 min after intravenous injection of 11 MBq/kg of ^{99m}Tc-labelled red blood cells (RBCs). The in vivo RBC labelling technique was used. Images were obtained in the anterior and best septal LAO projections using a conventional camera-computer system equipped with an all-purpose low-energy collimator. The scintigraphic studies were interpreted by two experienced nuclear physicians (C.A.B. and F.H.H.) who where blinded to the clinical and laboratory data. Skeletal muscle uptake of ^{99m}Tc-PYP and ^{67}Ga were considered abnormal when the contrast between bone and adjacent soft tissue was decreased (Fig. 1). The images were visually graded as negative, mild, moderate and marked. The scoring system proposed by Parkey et al. [6] was modified to grade ^{99m}Tc-PYP cardiac uptake as follows: 0, no myocardial activity (no myocardial uptake); 1+, possible although minimal myocardial activity (myocardial uptake<ribs); 2+, definite although mild myocardial activity (myocardial uptake=ribs) (Fig. 2); 3+, moderate myocardial activity (ribs<myocardial uptake<sternum); 4+, intense myocardial activity (myocardial activity>sternum). The myocardial uptake of ^{67}Ga was visually graded as negative, mild or marked (Fig. 3). Wall motion performance on gated blood pool imaging was graded as normal, mild dysfunction or marked dysfunction. Ejection fractions below 50% were considered abnormal.

Results

Skeletal muscle involvement using ^{99m}Tc-PYP

Table 1 summarizes the clinical, laboratory and scintigraphic findings. Abnormal muscle uptake was observed

Table 1. Clinical, laboratory and scintigraphic data (*LVH* left ventricular hypertrophy, *MI* myocardial infarction, *RBBB* right bundle branch block, *PR* short PR interval, *RBCD* right branch conduction defect, *ST* sinus tachycardia, *ST-T* non-specific ST-T changes, *EF* ejection fraction, – not done)

Patient	Clinical stage	CPK (U/L)[a]	LDH (U/L)[b]	SGOT (U/L)[c]	Muscle PYP	Muscle Ga	Heart PYP	Heart Ga	X-ray (cardiomegaly)	ECG	Gated blood pool	
											EF[d]	Motion
A.C.S.	IV	35	140	07	Normal	–	Score 0	–	Normal	PR	62%	Mild
M.S.O.	IV	41	183	19	Normal	–	Score 0	–	Normal	Normal	59%	Normal
A.F.M.	III	124	360	09	Mild	–	Score 0	–	Mild	ST, ST-T	64%	Normal
E.F.S.	III	262	399	11	Mild	–	Score 0	–	Normal	Normal	64%	Normal
H.H.O.	II	545	456	–	Marked	–	Score 3+	–	Mild	RBBB	48%	Mild
J.E.S.	III	99	629	12	Mild	–	Score 2+	–	Mild	LVH, ST-T	56%	Mild
M.S.	IV	112	729	20	Mild	–	Score 1+	–	Normal	Normal	63%	Mild
M.A.S.	I	2060	630	–	Marked	–	Score 3+	–	Marked	RBCD, ST, MI	25%	Marked
S.B.F.	III	69	430	18	Mild	–	Score 2+	–	Normal	ST-T	52%	Mild
T.M.M.	IV	34	690	15	Mild	–	Score 0	–	Normal	Normal	63%	Normal
A.P.E.	IV	36	220	08	Mild	Marked	Score 2+	Normal	Normal	Normal	55%	Normal
I.F.N.	III	28	213	15	Mild	Mild	Score 1+	Normal	Normal	ST, ST-T	62%	Normal
F.F.	IV	106	177	13	Mild	Mild	Score 0	Normal	Normal	Normal	71%	Normal
H.S.M.	IV	29	172	07	Mild	Mild	Score 2+	Mild	Normal	ST, ST-T	66%	Normal
M.N.P.	III	339	378	33	Moderate	Mild	Score 1+	Mild	Normal	Normal	51%	Mild
A.C.F.	III	15	334	07	Mild	Moderate	Score 1+	Normal	Normal	Normal	52%	Normal
L.C.S.	IV	101	388	30	Moderate	Moderate	Score 1+	Mild	Normal	Normal	62%	Normal
E.S.S.	IV	593	250	17	Mild	Marked	Score 0	Normal	Normal	Normal	67%	Normal
O.M.A:	IV	88	216	11	Mild	Mild	Score 1+	Normal	Normal	Normal	60%	Normal
M.A.L.	III	91	158	22	Moderate	Mild	Score 1+	Normal	Normal	ST-T	54%	Normal
R.R.S.	IV	147	236	09	Mild	Moderate	Score 1+	Normal	Normal	Normal	62%	Normal
L.A.N.	II	107	280	09	Mild	Mild	Score 0	Normal	Normal	ST-T	59%	Normal
A.A.J.	III	829	496	40	Mild	Moderate	Score 0	Normal	Normal	Normal	58%	Normal
L.O.	III	1725	509	38	Mild	Mild	Score 1+	Normal	Normal	ST	70%	Normal
D.A.F.	IV	24	134	13	Normal	Normal	Score 1+	Normal	Normal	Normal	59%	Normal
M.J.P.	IV	35	243	12	Normal	Normal	Score 2+	Normal	Normal	ST, ST-T	71%	Normal
M.S.C.	IV	27	202	08	Normal	Normal	Score 0	Normal	Normal	Normal	70%	Normal
E.M.P.	IV	13	214	19	Normal	Normal	Score 0	Normal	Normal	Normal	61%	Normal
T.V.S.	IV	26	190	08	Normal	Normal	Score 0	Normal	Normal	Normal	55%	Normal
A.A.A.	IV	46	157	05	Normal	Normal	Score 0	Normal	Normal	Normal	60%	Normal

[a] Normal values: 10–80 U/L (men) and 10–70 U/L (women); [b] Normal values: 120–248 U/L; [c] Normal values: up to 20 U/L; [d] Normal: 55%±5% (2SD)

Table 2. ^{99m}Tc-PYP scan in the skeletal muscle evaluation (n=30 pts, *NPV* negative predictive value, *PPV* positive predictive value)

	CPK (%)	LDH (%)	SGOT (%)	Clinical
Sensitivity	72.7	68.2	25.0	59.1
Specificity	100.0	100.0	100.0	100.0
NPV	100.0	100.0	100.0	100.0
PPV	57.1	53.3	34.8	47.1
Accuracy	80.0	76.7	46.3	70.0

Table 3. ^{67}Ga scan in the skeletal muscle evaluation (n=20 pts, *NPV* negative predictive value, *PPV* positive predictive value)

	CPK (%)	LDH (%)	SGOT (%)	Clinical
Sensitivity	71.3	50.0	35.7	50.0
Specificity	100.0	100.0	100.0	100.0
NPV	100.0	100.0	100.0	100.0
PPV	60.0	46.1	40.0	46.1
Accuracy	80.0	65.0	55.0	65.0

in 22 patients. Enzyme results confirmed the scintigraphic findings in 19 patients (86%). In contrast, clinical grading showed signs of active disease in only 13 patients.

Normal clinical status and enzyme results were observed in the eight patients with normal ^{99m}Tc-PYP scintigrams. Seven patients were indicated by abnormal enzyme levels and scintigraphy to have active disease, but this was not evident clinically. All were kept under corticosteroid therapy and subsequently showed normalization of laboratory and scintigraphic parameters. When scintigraphy was compared with CPK results, it showed 72.2% sensitivity, 100% specificity and 80% accuracy (Table 2). Scintigraphy showed poorer sensitivity (59.1%) but similar specificity in detecting the active phase of the disease when compared with clinical grading.

Skeletal muscle involvement using ^{67}Ga

Twenty patients underwent ^{67}Ga scintigraphy. Abnormal muscle uptake was seen in 14 cases (70%). ^{67}Ga scintigraphy showed similar results in detecting the inflammatory phase of the disease (Table 3). Although fewer patients were included in the analysis, a high negative predictive value was also observed.

Cardiac involvement

Table 4 summarizes the cardiologic findings. Cardiac ^{99m}Tc-PYP uptake was observed in 17 patients. The images were graded as 1+ in ten, 2+ in five and 3+ in two

Table 4. Cardiac findings (x abnormal studies, X total number of studies)

	ECG (x/X)	X-ray (x/X)	Gated (x/X)	Evolution
^{99m}Tc-PYP (n=30)				
10 pts score 1+	4/10	0/10	1/10	Good
5 pts score 2+	4/5	1/5	2/5	Good
2 pts score 3+	2/2	2/2	2/2	Died
^{67}Ga (n=20)				
3 pts mild	2/3	0/3	1/3	Good

patients. The two patients with a myocardial score of 3+ showed severe ECG abnormalities and intense left ventricular dysfunction on gated blood pool imaging. These two patients died and their autopsy results showed perivascular and interstitial mononuclear infiltrates, degeneration of muscle fibres and fibrosis in the myocardium. No changes were seen in the conduction system and coronary arteries. The remaining 15 patients with a score of ≤2+ did well with corticosteroid treatment. A close association was found betwen the magnitude of ^{99m}Tc-PYP myocardium uptake and the frequency or severity of ECG changes (P<0.01).

Gated blood pool studies showed mild wall motion abnormalities with normal left ventricular ejection fraction in five patients. This finding was also associated with a good clinical outcome.

Abnormal uptake of ^{67}Ga was seen in only 3 of 20 patients studied (15%). It is important to mention that the two patients who showed a ^{99m}Tc-PYP score of 3+ did not undergo a ^{67}Ga scan.

In summary, ^{99m}Tc-PYP myocardial scan was the most sensitive method in detecting cardiac abnormalities (57%), followed by ECG (40%) and gated blood pool (23%).

Discussion

Phosphate derivative tracers such as ^{99m}Tc-PYP, used for bone imaging, can be taken up by some soft tissue lesions. Several mechanisms have been proposed to explain this: (1) new bone formation and tracer adsorption to calcified tissue; (2) concentration in infarcted tissues due to adsorption to calcium ions present in high concentration in necrotic cells; (3) binding to hydroxyapatite and calcium phosphate crystals in ischaemic tissues; (4) binding to denatured proteins and other macromolecules in malignant neoplasms [7].

Our investigation showed a similar performance of ^{99m}Tc-PYP and ^{67}Ga in the evaluation of skeletal muscle. This might suggest that there is a coexistence of degenerative and inflammatory features in the skeletal muscle involvement in PM/DM. Moreover, considering the high specificity and negative predictive values ob-

tained (100%), the use of scintigraphy in monitoring the inflammatory activity of PM/DM might be of value when there is discordance between clinical and laboratory findings.

There have been a few studies on the use of polyphosphates in the detection of cardiac involvement in PM/DM. Duska et al., studying eight patients with PM/DM, found cardiac uptake of ^{99m}Tc-PYP in four of them [8]. Askari and Huettner detected myocarditis in two of five patients with PM/DM, based on abnormal ejection fractions on gated blood pool imaging [9]. Gottdienner et al., in a prospective study of 21 patients with PM/DM, found ECG, phonocardiographic and scintigraphic changes in 76% of them [10]. Previously, our group reported abnormal ^{99m}Tc-PYP heart scans in five of ten patients [11]. These patients were also included in the present analysis.

^{99m}Tc-PYP was the most sensitive tracer for detecting cardiac abnormalities (57%). Patients with a myocardial uptake score of 3+ had a poor outcome, while patients with a myocardial score of ≤2+ did well receiving corticosteroid therapy. This might suggest that ^{99m}Tc-PYP myocardial scan is of prognostic value.

^{67}Ga scan showed a low frequency of cardiac abnormalities. This might be explained by the fact that no patients in the acute phase of the disease underwent ^{67}Ga scan. The limitations of gallium for the detection of chronic inflammatory disease are well known.

The addition of ^{99m}Tc-labelled RBC gated blood pool imaging was not helpful in confirming the diagnosis of cardiac involvement by ^{99m}Tc-PYP scan. Furthermore, the exact clinical meaning of the mild kinetic ventricular dysfunction observed in five of our patients remains to be determined.

In conclusion, ^{99m}Tc-PYP and ^{67}Ga showed high accuracy in the detection of skeletal muscle involvement in PM/DM when compared with the conventional methods used in clinical practice. Their high negative predictive values indicate a potential clinical indication in the evaluation of inflammatory activity, especially in situations in which there is discordance between clinical and laboratory findings.

^{99m}Tc-PYP heart scan seems to permit early detection of cardiac involvement in PM/DM, especially in asymptomatic forms of the disease.

References

1. Plotz PH, Dalakas M, Leff RL, Love LA, Miller FW, Cronin ME. Current concepts in the idiopathic inflammatory myopathies: polymyositis, dermatomyositis, and related disorders (NIH Conference). *Ann Intern Med* 1989; 111: 143–157.
2. Kagen LJ, Aram S. Creatine kinase activity inhibitor in sera from patients with muscle diseases. *Arthritis Rheum* 1987; 30: 213–217.
3. Oppeinheim H. Zur Dermatomyositis. *Berl Klin Wochenschr* 1899; 36: 805–807.
4. Bohan A, Peter JB, Bowman RL, Pearson CM. A computer-assisted analysis of 153 patients with polymyositis and dermatomyositis. *Medicine* 1977; 56: 255–286.
5. Riddock G, Bristow WR, Cairns HWB, et al. Aids to the investigation of peripheral nerve injuries. Memorandum. *Medical Research Council* 1943; 7: 1–17.
6. Parkey RW, Bonte FJ, Buja LM, Stokely EM, Willerson JT. Myocardial infarct imaging with technetium-99m phosphates. *Semin Nucl Med* 1977; 7: 15–28.
7. Rosenthall L, Lisbona R. Extraskeletal localization of radiophosphate. In: Rosenthal L, Lisbona R., eds. *Skeletal imaging*. Norwalk: Appleton-Century-Crofts; 1984: 261–291.
8. Duska F, Bradna P, Pospisil M, et al. Pyrophosphate scintigraphy and other non-invasive methods in the detectin of cardiac involvement in some systemic connective tissue diseases. *Nucl Med* 1987; 26: 28–32.
9. Askari AD, Huettner TL. Cardiac abnormalities in polymyositis/dermatomyositis. *Semin Arthritis Rheum* 1982; 12: 208–219.
10. Gottdienner J, Sherber H, Hawley R. Cardiac Manifestations in polymyositis. *Am J Cardiol* 1978; 41: 1141–1149.
11. Buchpiguel CA, Roizenblatt S, Lucena-Fernandes MF, et al. Radioisotopic assessment of peripheral and cardiac muscle involvement and dysfunction in polymyositis/dermatomyositis. *J Rheumatol* 1991; 18: 1359–1363.