Scintigraphic Evaluation of Muscle Damage Following Extreme Exercise: Concise Communication

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Total body Tc-99m pyrophosphate scintigraphy was performed on 11 "ultramarathon" runners to assess the ability of nuclear medicine techniques to evaluate skeletal-muscle injury due to exercise. We found increased muscle radionuclide concentration in 90% of the runners. The pattern of muscle uptake correlated with the regions of maximum pain. The detection of exercise-induced rhabdomyolysis appeared to be best when scintigraphy was performed within 48 hr after the race, and to be almost undetectable after about a week. It was possible to differentiate muscle injury from joint and osseous abnormalities such as bone infarct or stress fracture. Although 77% of the runners had elevated serum creatine kinase MB activity, cardiac scintigraphy showed no evidence of myocardial injury.

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This study was performed to assess the ability of nuclear medicine techniques to evaluate skeletal-muscle injury following extreme exercise. We also attempted to determine whether muscle injury could be differentiated from osseous injury, such as stress fractures, in runners complaining of pain. The study included total-body imaging with Tc-99m pyrophosphate (Tc-PP) as well as detailed scintigrams of the muscles, joints, and bones of the lower extremities.

Extreme exercise has been found to be associated with elevated levels of serum creatine kinase (CK) and its MB isoenzyme (*1–7*). We performed myocardial scintigraphy to determine whether the runners with elevated serum CK activity showed any evidence of myocardial injury.

MATERIAL AND METHODS

We studied eleven well-trained and experienced runners, ranging in age from 27 to 64 yr, who competed in either a 50-mile or 100-mile "ultramarathon" foot race, four in the former and seven in the latter. The training regimen of the runners was from 20 to 60 miles per week for at least a year, with seven of the runners having completed at least one standard marathon run during the six months before this study.

Technetium 99m pyrophosphate scintigrams were obtained before the race on four runners, 24–48 hr after the race on all eleven runners, and from 4 to 8 days after the race on four runners. The scintigrams included four-view cardiac studies, total-body scans, and spot views of the lower extremities. A scintillation camera with a high-resolution collimator was used. All runners received ~20 mCi Tc-PP, and all studies were performed ~3 hr after injection.

An exercise history was obtained on the runners, including miles completed and the amount of pain experienced. Pain was rated from "0" for no pain to "4+" for severe pain.

The scintigrams were also rated on a scale of "0" to "4+," with "0" indicating no muscle uptake and "4+" indicating muscle uptake equivalent to, or greater than that in the most intense adjacent osseous structures. The scintigrams were interpreted without knowledge of the amount of pain experienced by the individual runners. Total CK values were measured and isoenzymes were separated by agarose gel electrophoresis and quantitated by fluorometric densitometry.

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TABLE 1.

Runner no.	Miles completed	Muscle pain experienced	Tc-PP Muscle uptake
1	100	4+	4+
2	100	3+	4+
3	100	3+	3+
4	100	2+	3+
5	100	1+	2+
6	100	0	0
7	90	1+	2+
8	50	4+	4+
9	50	3+	3+
10	50	2+	2+
11	50	1+	3+

RESULTS

All four runners who competed in the 50-mile race completed the entire course. Six of the 100-mile runners completed the course, but one runner was forced to stop running because of a foot injury at 90 miles. Table I summarizes the pain symptoms, running history, and Tc-PPi muscle uptake. The table also shows that muscle uptake of the tracer correlated in general with the site of the pain experienced by the runners. Ninety percent of the studies performed 24 to 48 hr after the race were abnormal, showing increased tracer deposition in the leg muscles. The only normal study was in the runner who did not complain of pain after completing the 100-mile race. All studies before the race were normal.

Figure 1 shows the scintigrams of Runner 3, who completed the 100-mile race. He experienced moderately severe pain in his thighs during the race and had 3+ Tc-PPi muscle uptake. Figure 1 (left) was obtained 24 hr after the race; it shows significant concentration of Tc-PPi in the hamstring and quadriceps muscles. Figure 1 (right) is his repeat scintigram seven days later. This study was normal.

Figure 2 (left) is the 24-hr scintigram of Runner 8 who completed the 50-mile race. He experienced 4+ pain, and his scintigram is also rated 4+. It shows considerably increased uptake in the adductor muscles of the thighs. Figure 2 (right) is his repeat study, performed three days later. It shows continued uptake in the adductor muscles, although significantly less than in the 24-hr postrace study.

The immediate postrace serum CK activity was elevated in all of the runners, ranging from 485 to 34,130 IU/l, with a mean of 8,640 IU/l. Serum CK-MB activity was elevated in eight (77%) of the runners. The range was 37 to 2,049 IU/l, with a mean of 279 IU/l.

The follow-up studies performed within five days of the race demonstrated abnormal muscle uptake, although the degree of abnormality was less than that found in the muscles of the same runners shortly after the race. Follow-up studies at seven and eight days after the race were normal.

We found that the different muscle stresses in running uphill or downhill caused different muscle groups to be detected as abnormal. Uphill running produced increased Tc-PP deposition primarily in the adductor muscles of the thigh, whereas runners who ran the predominantly downhill 100-mile race showed abnormalities in the hamstring, quadriceps, and buttock muscles. Only one of the runners had an abnormal postrace skeletal scintigram. He showed increased uptake in the mid shaft of a femur, thought to represent a bone infarct that had occurred during a previous ultramarathon race. He did not experience pain in the region of the scintigraphic abnormality during the current race but had felt a sharp pain in this area approximately two months previously.

Nine of the runners (82%) had some degree of increased Tc-PPi concentration in the ankles and knees. This did not appear to decrease significantly in the delayed scintigrams. All cardiac scans were completely normal.

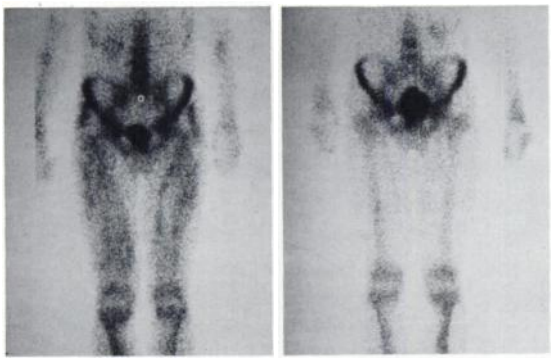

FIG. 1 Anterior whole body scintigrams of a runner who completed a 100-mile foot race. Race was primarily downhill. It shows increased concentration of Tc-99m pyrophosphate in painful injured muscles of buttocks, quadricep group, and hamstrings (left). Study was performed 24 hr after completion of race. Follow-up study of same runner at 8 days after the race (right). There is no evidence of increased muscle uptake.

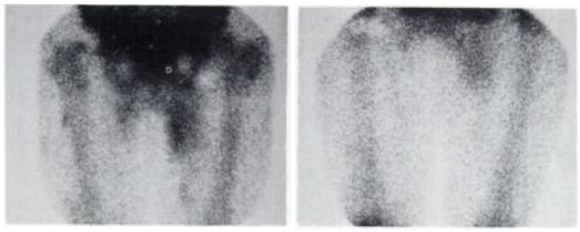

FIG. 2 Anterior view scintigraphs of thighs of runner who completed a 50-mile foot race. Race was primarily uphill. PPi scintigram obtained 24 hr after completion of race shows increased concentration of pyrophosphate in painful injured adductor muscles, primarily on left (left). Follow-up study was performed 4 days after race (right). Abnormal muscle uptake is still seen, but it is significantly less pronounced than in the 24-hr study.

DISCUSSION

Starting in 1979, we began obtaining blood samples from runners participating in a 100-mile ultramarathon foot race known as the "Western States 100 Miler". The race starts at the base of Squaw Valley ski area at an elevation of 6200 feet, and proceeds over the top of the ski area at elevation 9000 feet before continuing on an up-and-down course over peaks and valleys until its termination at Auburn, California, at elevation 1200 feet. This exhausting race provided us with considerable information pertaining to the effects of extreme exercise on humans.

Among the many interesting findings, we noted that the serum creatine kinase activity was elevated to values over thirty times normal, and the MB isoenzyme, thought to be specific for cardiac damage, was elevated into the range usually associated with massive myocardial necrosis.

Our original theory was that myocardial damage was being caused by relative myocardial ischemia or by damage to the myocardium produced by the running 100 continuous miles. We also considered the possibility of skeletal-muscle damage, since almost all runners complained of pain and there were a few reports in the literature about elevated CK-MB in conditions other than myocardial necrosis. (*8*,*9*)

We performed cardiac and total-body scintigraphy on seven runners from the 100-mile race and four runners who completed a 50-mile footrace from Sacramento to Auburn, California. The latter is primarily an uphill race, starting at sea level and ending at ~1200 feet. Following the previously described protocol, we found increased uptake of Tc-PP in the leg muscles of the runners. The involved muscles were different in the 100-mile race (primarily a downhill race) from those in the mainly uphill 50-mile race. The 100-mile runners showed primary involvement of the buttock, hamstring and quadriceps groups, whereas, the 50-mile runners had most abnormalities in the thigh adductor muscles. Elevated serum CK levels were present in all of the runners, and elevated CK-MB isoenzyme activity was present in 77% of them. We also found that the time course of abnormal skeletal-muscle uptake appeared to be similar to that of the technetium bone-imaging agents in myocardial infarcts. The skeletal-muscle abnormalities were apparent on the scan about a day after injury and were no longer detected when imaging was performed about a week after the race.

Although almost all of the runners complained of pain, including some in whom it was quite severe, we found no evidence of stress fractures or severe joint problems. There was increased tracer concentration in the joint regions in nine of the eleven runners but it was in the minimal-to-moderate range. The presence of increased Tc-PP concentration in the muscles did not preclude visualization of the skeletal structures, although in some runners additional projections were required. We concluded that stress fractures, joint abnormalities, and rhabdomyolysis can be differentiated easily from each other. This should be helpful in determining the causes of pain in patients following exercise.

The mechanism of deposition of the bone-seeking agents in injured skeletal muscle is probably similar to that of myocardial uptake following infarction or injury (*10*). As described by Brill (*11*) in his recent review, possible mechanisms include hyperemia, adsorption onto soft tissue calcium, binding by tissue hormone or enzyme receptors, tagging to denatured proteins, altered capillary permeability, and adsorption onto immature collagen. Most likely, one or more of the above mechanisms come into play when skeletal muscle tissues are damaged. Buja et al (*12*) have shown by electron microscopy that technetium phosphates do adsorb onto calcium hydroxyapatite, amorphous calcium phosphates and calcium complexed with certain macromolecules.

Included among the practical aspects of this study is the detection of skeletal muscle necrosis following exercise. This represents a very useful and essentially new imaging modality for nuclear medicine departments, especially those where referring physicians are interested in sports medicine and trauma. Imaging with the technetium phosphates should help to differentiate between muscle and skeletal injuries in many cases.

Another practical finding is that myocardial scintigraphy may be the only reliable means of detecting a postexercise myocardial infarction. In many cases, the patient may have an abnormal or nondiagnostic electrocardiogram, due to exercise or other cause. The knowledge that elevation of serum CK-MB activity may be due to skeletal muscle injury further complicates the situation, since this isoenzyme had been thought to be specific for cardiac damage. It has been argued that microscopic myocardial damage may produce elevations of CK-MB and not be detected by scintigraphy, but it is very unlikely that microscopic cardiac damage could cause the tremendously elevated serum CK-MB activity that we found in the runners (*13*).

From this study we can assume that some runners who have been diagnosed as having a myocardial infarction probably carry this label unnecessarily.

A final practical issue, although subjective, is that the runners who complain of the most severe pain, in general, have the most abnormal scintigrams. This indicates that these athletes should probably have a greater amount of rest before resuming a training regimen than runners who do not complain of significant pain, or whose scintigrams are normal or only minimally abnormal.

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The Education and Research Foundation of the Society of Nuclear Medicine Fellowship/Pilot Research Grant

The Education and Research Foundation of the Society of Nuclear Medicine welcomes applications for Student Fellowships and Pilot Research grants. These awards are made possible through donations from SNM members as well as from various commercial firms whose products are used in the practice of Nuclear Medicine. Applications received prior to December 15 of any year will be evaluated by the ERF Board on a competitive basis. Awards will be announced on or about February 15 of the following year.

STUDENT FELLOWSHIP GRANTS

These awards are designed to stimulate interest among students in the United States and Canada in the field of Nuclear Medicine. The awards are intended to provide an opportunity to spend elective quarters and/or summers in active departments working and associating with experts in the field. Maximum grant: $1,500. Letters of application should be submitted in duplicate and should contain the following: applicant's name, address, birth date, period for which support is requested, name and institution of sponsor, previous education, previous research, and brief summary of the proposed project, including an appropriate bibliography. Application forms should be requested from the office of the E&R Foundation. Additional applications may be submitted prior to May 1, 1983.

PILOT RESEARCH GRANTS

The goal of this research support is to provide money to young scientists working in Nuclear Medicine who desire support for a research project. Priority will be given to those proposals that are of a pilot nature in either clinical or basic research. The grants are not intended to support salaries, purchase major equipment, or for travel, but are designed to provide essential materials so that innovative ideas can be quickly tested. Maximum grant: $3,000. Additional applications may be submitted prior to May 1, 1983.

SPECIAL ANNOUNCEMENT: THIRD TETALMAN MEMORIAL AWARD

A fund has been established in the ERF by friends of Marc Tetalman, M.D., who was a tragic homicide victim while attending the SNM meeting in Atlanta in June 1979. This fund will permit an award of $3,000 to be made in June, 1983 to a young investigator (35 years of age or younger) who is pursuing a career in Nuclear Medicine. This award is to be repeated annually. It is possible that additional contributions to our fund will permit the stipend to be increased in future years. Applicants should submit prior to March 1, 1983 a curriculum vitae together with data supporting current research efforts.

All letters and applications should be addressed to:

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