Tc-99m Pyrophosphate Muscle Labeling in McArdle Syndrome

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This paper reports the findings on two patients with McArdle syndrome (myophosphorylase deficiency) in whom conventional bone scans with Tc-99m pyrophosphate revealed intense muscle labeling following exercise tests. The temporal pattern observed was similar to that seen with other types of muscle damage. The prolonged cramps often occurring with this entity appear to produce muscle damage that is readily demonstrable using conventional bone-scanning techniques.

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This paper reports two cases of McArdle syndrome (myophosphorylase deficiency) in which bone scans revealed intense muscle labeling following exercise tests.

McArdle syndrome is an inherited disorder characterized by painful muscle cramps following exercise. This often leads to myoglobinuria and occasionally to renal failure (*1*). Skeletal muscle from affected individuals lacks the enzyme phosphorylase, which prevents the degradation of muscle glycogen to lactic acid (*2*). It has been suggested that the failure to produce glucose from glycogen during exercise impairs the energy-dependent recovery of calcium by the sarcoplasmic reticulum, an essential step in the process through which a contracted muscle cell relaxes (*3*).

The "ischemic exercise test" is used to determine whether the ability to convert muscle glycogen to lactic acid is impaired. It is performed by applying a tourniquet above the elbow and having the patient exercise the forearm muscles vigorously for 1 min. The change in lactic acid content of venous blood before and after exercise is measured. Normally the lactic acid content is significantly increased. In patients with McArdle syndrome there is little or no change.

In the cases reported below, bone scans done after the "ischemic exercise test" showed intense labeling of the involved muscle groups.

CASE REPORTS

Case 1. A 38-year-old man had a 10-yr history of painful muscle cramping following moderate exercise. On several occasions exercise was followed by dark urine, and on one occasion acute renal failure occurred, from which he recovered after hemodialysis. Serum creatine phosphokinase (CPK) on that occasion was 60,000 (normal <60 mU/ml). Two sisters, both examined by the authors, were similarly affected.

Physical examination was normal except for wasting and slight weakness of the left thigh, the result of an episode of severe cramping and myoglobinuria 1 mo before. Routine laboratory data were normal, except for CPK of 629, serum glutamic-oxaloacetic transaminase (SGOT) of 83 (normal <50 mU/ml), and aldolase of 14 (normal <12 mU/ml). Urine was negative for myoglobin. Electromyography revealed mild changes compatible with a myopathy. Biopsy of the left quadriceps muscle revealed total absence of muscle phosphorylase activity; subsarcolemmal blebs occurred in many fibers and there were mild myopathic changes.

McArdle syndrome was suspected. With the cir-

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culation occluded by a blood-pressure cuff inflated to 100 mm Hg above systolic blood pressure, the subject was instructed to open and close the hand repeatedly against a thick roll of gauze held in the palm. This ischemic exercise resulted in no increase in lactic acid concentration of venous blood obtained from antecubital vein (pre-exercise 20 mg/dl, post-exercise 19 mg/dl). Normal values for three volunteers were 5–20 mg/dl with four- to sevenfold increase in lactic acid following ischemic exercise. During the ischemic exercise test the patient developed a painful cramp involving the long flexor muscles of the digits and wrist on the ulnar side of the forearm. The cramp, which by electromyographic needle examination was electrically silent, lasted 20 min. During this time the digits could not be voluntarily or passively extended.

A conventional bone scan was carried out 22 hr after the ischemic exercise test and 3 hr after the i.v. administration of 20 mCi of Tc-99m pyrophosphate. It revealed labeling sharply limited to the forearm muscles involved in the cramp (Fig. 1A, B). The only other unusual activity was a small faint area of increased labeling in the left thigh, the site of a muscle biopsy performed 24 hr before the bone scan. The osseous structures appeared to label normally.

Case 2. A 45-year-old woman (sister of Case 1) had a 25-yr history of weakness, stiffness, pain, and muscle swelling following exercise. Twenty-three years before, she had an episode of dark urine followed by renal failure. She also had angina pectoris.

Physical examination was normal except for slight weakness of the muscle of the thigh and pelvic girdle. Routine laboratory data were normal, except for CPK of 650 and aldolase of 13. SGOT was 40, and urine was negative for myoglobin. Electromyography was as in Case 1. Biopsy of the left deltoid muscle revealed no muscle phosphorylase activity. Subsarcolemmal blebs were present.

McArdle syndrome was suspected. An ischemic exercise test resulted in no significant increase in lactic acid (pre-exercise 8.3 mg/dl, post-exercise 10.9 mg/dl). An electrically silent painful cramp of forearm muscles occurred during the ischemic exercise test. The cramp lasted for 11 min, and the pain for several days.

Two Tc-99m pyrophosphate scans were done on this patient. The first, carried out 24 hr after the ischemic exercise test, yielded findings identical to those in Case 1 (Fig. 2, left). The second, done 9 days later, showed interval clearing of the abnormal labeling of the flexor muscles of the forearm but now there was abnormal activity in the medial heads of both gastrocnemius muscles (Fig. 2, right). Subsequent investigation revealed that on the day before the scan she had experienced cramps in these muscles while exercising on a treadmill during stress electrocardiography.

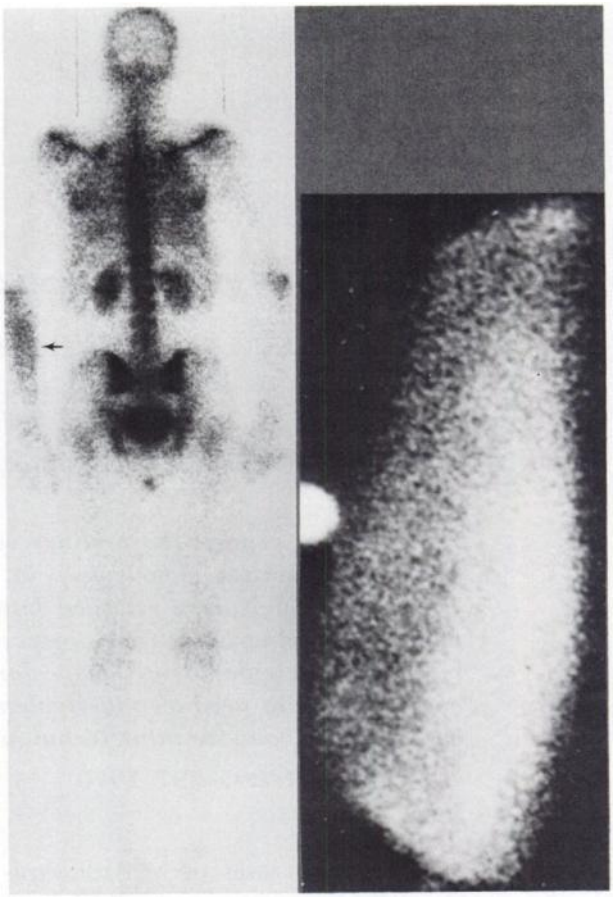

FIG. 1. Case 1. Left—Posterior rectilinear bone scan obtained 2 hr after i.v. administration of Tc-99m pyrophosphate and 22 hr after ischemic exercise test of left arm. Note intense labeling of long flexor muscles of left forearm. Right—Gamma-camera image of volar aspect of left forearm.

DISCUSSION

These studies were carried out as part of an ongoing project designed to determine the utility of conventional Tc-99m pyrophosphate bone scanning in inflammatory myopathy. We have noted increased muscle uptake of T-99m pyrophosphate in these patients, the uptake being most intense in the muscles clinically affected, and clearing after treatment with corticosteroids (*4,5*). This has also been observed by others in experimental and clinical studies (*6–8*). The mechanisms that resulted in the radioactive labeling of the damaged muscle are poorly understood but are thought to be similar to the processes that cause labeling of irreversibly damaged myocardium following acute infarction (*9,10*), in

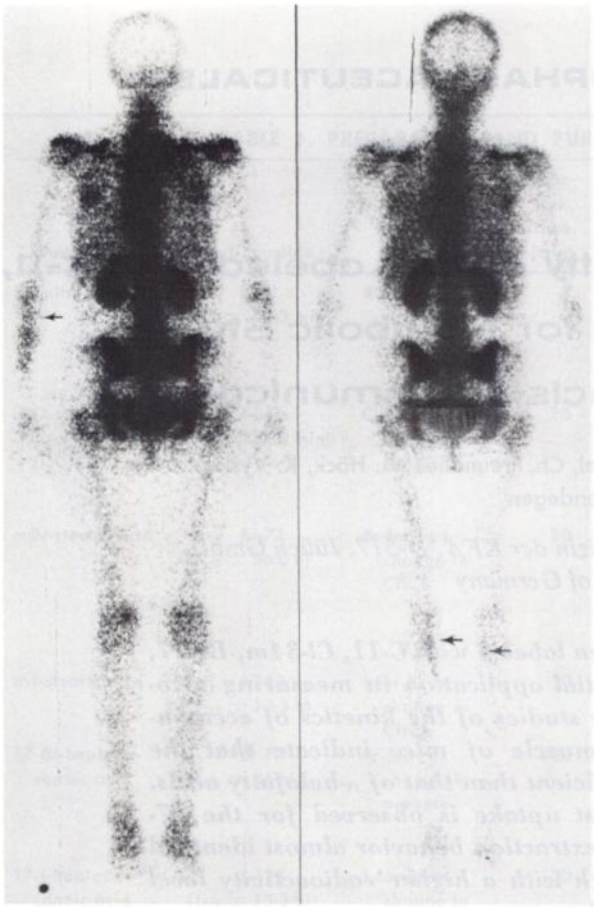

FIG. 2. Left—One day after ischemic exercise test. Right—Nine days later (1 day after sustaining cramps in both calves during stress electrocardiography). Note that earlier labeling of muscles of left forearm has cleared, and that there is now labeling in heads of both gastrocnemius muscles.

which labeling appears to follow shifts in muscle calcium.

In McArdle syndrome, the ischemic exercise may cause damage to components of myofibers, with secondary accumulation of calcium resulting in labeling by Tc-99m pyrophosphate.

Another possible mechanism producing labeling unique to McArdle syndrome involves the postulated failure of the sarcoplasmic reticulum to reaccumulate calcium in this disease (*3*). This could raise sarcoplasmic calcium concentration and produce the labeling observed as well as the persistent contracture that is the hallmark of the syndrome.

CONCLUSION

Nuclear medicine physicians should add McArdle syndrome to the growing list of entities to be considered when focal soft-tissue labeling is noted on a bone scan. They should also be aware that muscle scanning with Tc-99m pyrophosphate can be used to demonstrate the location and extent of the muscle injury in patients with this entity.

ADDENDUM

Since the submission of this manuscript an abstract has appeared describing increased uptake of Tc-99m diphosphonate in myophosphorylase deficiency. KULA RW, BRUMBACK RA, ENGEL WK, et al: Ischemic contracture in muscle phosphorylase deficiency: Clinical scanning and histochemical and autoradiographic studies. *Neurology* 27: 401–402, 1977 (Abst)

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