Summary. This report concerns two unrelated males; one had sarcoidosis, sarcoid myopathy and muscle weakness, and the other had exercise-induced weakness and myalgia. Both patients had a lack of ammonia rise in their serum after an ischemic work test, minimal histochemical activity of myoadenylate deaminase in repeated muscle biopsies, and less than 5% of normal biochemical activity of myoadenylate deaminase in their skeletal muscles. These three criteria establish primary myoadenylate deaminase deficiency as a separate primary metabolic muscle disease which merits differential diagnostic consideration when patients complain of muscle weakness and cramps.

Key words: Myoadenylate deaminase deficiency – Histochemistry – Biochemistry – Metabolic myopathy

Several enzyme deficiencies are now known to cause hereditary neuromuscular diseases. Although myoadenylate deaminase deficiency (MADD) is one of the most recently detected (Fishbein et al. 1978), it is probably the most often encountered enzyme defect among neuromuscular disorders (Fishbein et al. 1984). The clinical picture may be characterized by weakness and muscle cramps (Kelemen et al. 1982), but its seems to be of great variability (DiMauro et al. 1980; Swain et al. 1983).

Biochemically, patients completely lack the enzyme myoadenylate deaminase (MAD) in their muscle tissues. This enzyme catalyses the deamination of adenosine monophosphate (AMP) to inosine monophosphate (IMP), thereby liberating ammonia which may be measured both in muscle tissue and in serum. The mechanism leading to the clinical symptomatology of weakness and muscle cramps has not been fully elucidated. Possibly the low removal of AMP caused by MADD may shift the myokinase reaction $2 \text{ADP (adenosine diphosphate)} \rightleftharpoons 1 \text{ATP (adenosine triphosphate)} + 1 \text{AMP toward ADP}$. Under certain conditions this may lead to low ATP values and an energy deficit (Swain et al. 1983).

The histochemical absence of myoadenylate deaminase has often been encountered in well-defined neuromuscular disorders, such as dermatomyositis and systemic sclerosis (Kar and Pearson 1981) or neurogenic atrophy (Shumate et al. 1979). Histochemical MADD has also been considered a primary and thus separate nosological entity (Kelemen et al. 1982).

We report findings in two unrelated male patients whose original histochemical demonstration of MADD was subsequently confirmed by biochemical analysis, both in ischemic work tests and by biochemical determination of MAD activity in their muscle tissues.

Materials and Methods

Five muscle biopsies taken 6 and 23 months apart from patient 1, and two biopsies taken 5 months apart from patient 2 were available for morphological studies. Parts of the muscle specimens were
Fig. 1. In patient 1, the ischemic work test reveals a normal increase of lactate (open triangles) as compared to 12 control individuals (full circles), upper curves, but virtually no production of ammonia in the MAD-deficient patient (flat baseline marked by open triangles) as compared to the regular rise in ammonia of 12 normal control individuals (full circles), during a 20-min post-ischemic period, lower curves.

Histochemical MAD preparation was performed according to the original method (Fishbein et al. 1980), with incubation for 1 h. Later incubation was extended to 3 h in all our specimens. For control purposes muscle specimens of patients with various neuromuscular conditions were processed under identical conditions.

One muscle biopsy specimen from each patient was immediately frozen in liquid nitrogen at the time of surgical removal for biochemical determination of MAD activity (DiMauro et al. 1980). The muscle biopsy specimen of patient 1 was taken from the second series of muscle biopsies.

**Patient 1**

This 60-year-old male patient had had pulmonary sarcoidosis since 1950 and had been repeatedly treated with steroids. In the fall of 1981 he experienced lumbar pain radiating into his right leg. Under conservative, i.e. drug and physical therapy, it subsided. However, at this time and possibly even earlier, the patient noted easy fatigability of his leg muscles after prolonged walking, especially when climbing stairs or walking up a hill.

Neurological examination showed moderate atrophy of his leg and biceps. Deep tendon reflexes of both legs were reduced. He had marked weakness of his lower leg and elbow flexor muscles, and moderate weakness of quadriceps and pelvic girdle muscles. He had no sensory deficits but reduced vibration sense in his toe regions.

Electromyography revealed abnormal spontaneous activity, fibrillation, positive sharp waves, and reduced interference patterns in the tibialis anterior, gastrocnemius, quadriceps, deltoid, and biceps muscles, and myotonic discharges and polyphasic potentials of reduced amplitude especially in the quadriceps and biceps. Motor nerve conduction velocities of the peroneal nerve was 44 m/s, of the right median nerve 52 m/s, and sensory nerve conduction velocity of the right sural nerve was 46.5 m/s. All values were considered to be within normal limits. Creatine kinase was always slightly elevated.

Angiotensin converting enzyme activity (ACE) was temporarily elevated to 171 nmol/min/ml (nor-