Case Report

Adult Form Acid Maltase Deficiency
—A Case Report—

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The case of a 26 year old man with acute respiratory difficulty was reported. Morphological and biochemical analysis of biopsied gastrocnemius muscle indicated a diagnosis of adult form acid maltase deficiency. Clinically, the most interesting point of our case was the presence of a thickening of the posterior papillary muscles and chordae without any functional disturbance, which was detected by echocardiogram. Another interesting point of our case was the existence of a sibling who died of progressive muscular dystrophy at the age of 31 years. This may raise the possibility that we are dealing with a familial type of adult form acid maltase deficiency.

Key words: Adult form, Acid maltase deficiency, Muscle biopsy, Respiratory failure, Echocardiogram, Familial involvement.

Acid maltase deficiency (AMD) is characterized by accumulation of glycogen in numerous tissues. It affects infants and children, with a few cases occurring in adults. An adult patient initially has progressive muscular weakness and respiratory dysfunction as symptoms. However, those symptoms also frequently occur in the course of neuromuscular disease. The clinical diagnosis of an adult patient with AMD may be difficult or missed because of similarities to other myopathies such as polymyositis or limb girdle muscular dystrophy. Thus, careful evaluation of histopathological and biochemical analysis is necessary to diagnose AMD in adults. The study of muscle biopsy specimens eventually led to the correct diagnosis.

This report describes a patient with the adult form of AMD, as proved by muscle biopsy, whose echocardiogram suggested a marked deposit of glycogen in the posterior papillary muscles and chordae.

CASE REPORT

Present Illness

A 26 year old man was admitted to Ehime Central Prefectural Hospital in August 1980 with dyspnea and difficulty in producing sputum. Four days before admission he had had a cold. Dyspnea and high fever (38-39°C) became worse. He was transferred to the emergency room. Blood gas studies at that time showed hypoxemia (atrial oxygen tension PaO₂ 53 mmHg). The chest X-ray disclosed acute bronchopneumonia. Intensive care, including tracheostomy and intermittent positive pressure respiration, was administered for several weeks until his condition gradually improved. Confirming examinations were performed when he had recovered.
Past medical history

The patient's prenatal development, delivery, and postnatal development has been normal. He was first examined at a hospital at the age of 19 for scoliosis and gradually progressing muscle weakness. No definite diagnosis was made at that time. He got a job at age 22 as a bank employee. He had been employed without problem.

Family history

The parents were consanguineous (Fig. 1). The propositus had two siblings. The elder sister was healthy, but the elder brother died at the age of 31 from cardiopulmonary failure, and had been diagnosed as having progressive muscular dystrophy without muscle biopsies having been performed. The parents knew of no other cases of neuromuscular disorders in their families.

Physical examination

The patient was a short, poorly nourished man, weighing 39.5 kg and 155.5 cm tall (Fig. 2). Vital signs included blood pressure of 134/84 mmHg and pulse rate of 76 beats per minute. His intercostal muscles moved poorly in respiration. Manual muscle testing demonstrated moderate to severe weakness of the dorsal and intercostal muscles. Moderate weakness of the pelvic girdle and shoulder girdle muscles was evident. Slight weakness was noted in the other proximal limb muscles. His gait was almost normal, but he could not run fast. His tongue was

Fig. 1. Pedigree chart White = living and healthy. Black = dead; age and cause of death, if known, are shown. T.B. = tuberculosis, Apo. = apoplexy.

Fig. 2. Twenty-six year old man with AMD. Scoliosis is evident. Intercostal, scapular, dorsal, and gluteal muscles are decreased in bulk.
of normal size. Cardiac examination revealed no cardiomegaly, and heart sound was normal without any murmur. No rale was heard at any lung field but the breath sound somewhat weak. There was no hepatosplenomegaly. Neurological study revealed no abnormalities, and no pathological reflex was detected.

Laboratory examination

Laboratory findings included the following; serum glutamic oxaloacetic transaminase level, 54 to 89 units/dl (normal, 10 to 38 units/dl); glutamic pyruvic transaminase level, 31 to 89 units/dl (normal, 4 to 35 units/dl); aldolase level, 9 units/dl (normal, less than 11 units/dl); creatine phosphokinase (CPK) level, 325 to 450 international units/dl (normal, less than 82 international units/dl); CPK isozyme, BB type 0%, MB type 3%, MM type 97%; lactic dehydrogenase level, 521 to 626 units/dl (normal, 50 to 400 units/dl); serum electrolytes, within normal; immunoglobulins, within normal limits (range); serological examinations, normal; tri and tetra iodothyronines, within normal; cerebrospinal fluid, no abnormalities; kidney function and liver function tests, within normal; glucose tolerance test, glucagon and epinephrine tests, within normal. No abnormal levels were shown in creatinine, myoglobin and lactic acid. Serum lipids levels were almost normal except hypocholesterolemia (63 to 105 mg/dl). However, the serum lipoprotein electrophoretic attern appeared to be normal. Test of pulmonary function revealed a restrictive defect with a forced vital capacity (FVC) of 1.28 L (33.3% of predicted) and a forced expiratory volume in one second of 93.7% of FVC. The chest X-ray demonstrated a normal size heart with a cardiothoracic ratio of 35%. Electromyography showed an abnormal irritability of muscle fibers and myotonic discharges without clinically detectable myotonia. Electrocardiogram was normal. Echocardiogram revealed normal size chambers, valves, and contraction (Fig. 3). Two-dimensional echocardiogram distinctly showed located thickness of posterior papillary muscles and chordae (Fig. 4). This raises the possibility that glycogen was deposited in the region. Left gastrocnemius muscle biopsy was done for both biochemical and morphological studies.

Levels of acid and neutral α-1-4 gluc-
Fig. 4. Simultaneous recorded two-dimensional echocardiogram is shown. Findings are consistent with M-mode scanning. Abnormal echo of PPM which seems to infiltrate into the cardiac muscle is evident. Ao=aorta, LA=left atrium, PW=LVPW.

sidase in biopsy muscle and urine from the patient and control subjects were measured by the fluorimetric method employing 4-methyl-umbelliferyl-α-D-glucopyranoside (MUαG) as substrate\(^5\). In the muscle the level of acid maltase was extremely low; neutral maltase level was also low. In the patient’s urine acid maltase level was zero, neutral maltase level almost normal (Table 1).

Laboratory details of the family are summarized in Table 2. The brother had been examined at the age of 26, when he was diagnosed as having progressive muscular dystrophy. Mother and cousins had some abnormal laboratory findings, but they showed no clinical signs of AMD.

Light microscopy

On cryostat sections a number of histochemical and histoenzymatic stains were performed. Most muscle fibers contained multiple vacuoles of various size, which was the most prominent pathological finding (Fig. 5). Vacuoles appeared filled with a PAS-positive, basophilic amorphous material, which disappeared after digestion, indicating that it was glycogen. Vacuoles were highly reactive for the acid phosphatase, thus suggesting an autophagic activity. Vacuoles also reacted negatively for phospholyase, oxidative enzyme (i.e. NADH-TR), and lipid stains. The histo-

<table>
<thead>
<tr>
<th>Table 1. The acid and neutral maltase levels in the muscle and urine from the patient and controls.</th>
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<tbody>
<tr>
<td><strong>Patient Muscle</strong></td>
</tr>
<tr>
<td>Acid maltase (pH 4.0)</td>
</tr>
<tr>
<td>Neutral maltase (pH 6.5)</td>
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*: Results shown as nanomoles of 4-methyl-umbelliferone produced (MUP) per milligram protein per hour.

\^: Results shown as nanomoles of MUP per milligram creatinine per hour. MUαG as substrate.
Table 2. Serum enzyme assays of the family

<table>
<thead>
<tr>
<th></th>
<th>Father</th>
<th>Mother</th>
<th>Brother</th>
<th>Sister</th>
<th>Propositus</th>
<th>Cousin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S.M59y</td>
<td>S.M59y</td>
<td>S.M26y</td>
<td>Y.K31y</td>
<td>N.M26y</td>
<td>N.Ksy</td>
</tr>
<tr>
<td>GOT(10-38 ku)</td>
<td>23</td>
<td>10</td>
<td>324</td>
<td>6</td>
<td>67</td>
<td>18</td>
</tr>
<tr>
<td>GPT(4-35 ku)</td>
<td>28</td>
<td>8</td>
<td>160</td>
<td>6</td>
<td>45</td>
<td>8</td>
</tr>
<tr>
<td>LDH(50-400 ku)</td>
<td>363</td>
<td>481</td>
<td>#</td>
<td>#</td>
<td>#</td>
<td>#</td>
</tr>
<tr>
<td>CPK(51-514 u)</td>
<td>70</td>
<td>90</td>
<td>128.9</td>
<td>40</td>
<td>450</td>
<td>50</td>
</tr>
<tr>
<td>ALDase(3-8 u)</td>
<td>8</td>
<td>10</td>
<td>#</td>
<td>#</td>
<td>#</td>
<td>4</td>
</tr>
</tbody>
</table>

*: In each case, results of first determination are shown.
#: Abnormally high levels are marked.

Fig. 5. Light microscopic figures of gastrocnemius muscle. A number of fibers with intracytoplasmic vacuoles in various sizes (a) which are predominantly seen in type 2 (2) and rarely in type 1 (1) fibers (b). Both type 1 and type 2 fibers, especially type 2 fibers, are highly reactive for acid phosphatase staining (dark dots) (c). The vacuoles are filled with PAS positive materials (d). Serial frozen sections stained with Hematoxylin-Eosin (a), routine ATPase (b) and acid phosphatase (c). Epon-embedded semithin section stained with PAS (d). a-c: ×180, d: ×350.
pathological findings led to the diagnosis of late onset acid maltase deficiency.

Electron microscopy

Ultrastructural studies demonstrated the accumulation of excess glycogen and the presence of prominent autophagic vacuoles (Fig. 6).

DISCUSSION

Until recently, acid maltase deficiency was recognized as a fatal disease of infancy only, but a few sporadic cases have occurred in adults. In this type the weakness is selective in distribution; organomegaly is typically absent and the disease progresses slowly. In this disease respiratory muscles are selectively affected (one third of the adult AMD cases reported showed respiratory failure), and ventilatory failure may often be present, as in our case.

Furthermore, adult AMD is also known to be very difficult to diagnose clinically because of similarities to other myopathies. Therefore, it is important to evaluate both the histopathological and the biochemical analyses. Morphological findings in our case were vacuolar myopathy, which agrees with the typical adult AMD. The biochemical analysis of the biopsy specimens and urine was enough to diagnose our case as adult AMD.

There are few reports of echocardiographic studies in adult AMD. Cardiac physical examination and electrocardiogram of our case showed no abnormality, but the echocardiogram revealed hypertrophy of the posterior papillary muscles and chordae without functional disturbance. Unfortunately, histopathological analysis was not performed on cardiac muscle. However, the finding from echocardiogram raises the strong possibility that glycogen was deposited in the region.

Another interesting point of our case was the death of a sibling with progressive muscular dystrophy, whose clinical symptoms were extremely similar to those of our case. Although it is well known that acid
Adult form acid maltase deficiency

maltase deficiency is an autosomal recessive inherited disease\(^{11}\), there are few reports concerning adult AMD that suggest familial involvement\(^{12}\). Our case may indicate that we are dealing with a familial type of adult AMD.

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