persistent physiologic abnormalities in humans accidentally or industrially exposed to chlorine gas in various concentrations that could not be attributed to smoking or concomitant disease. Kowitz and associates documented increased elastic work of breathing, reduced diffusing capacity, and reduced vital capacity in 59 nonhospitalized dock workers and an elevated airway resistance in 11 hospitalized patients, which progressively improved towards normal. Chester et al were unable to conclusively show physiologic abnormalities in chlorine gas workers chronically exposed to concentrations of chlorine less than 1 ppm. A significant difference in the mean forced expiratory flow during the middle half of the FVC (FEF25-75%) was demonstrated between nonsmoking normal subjects not exposed to chlorine and chlorine gas workers who smoked. The effects of smoking made it impossible to attribute a reduction in FEF25-75% to exposure to chlorine alone when all groups were compared. All studies of short-term exposures have shown an initial obstructive ventilatory impairment associated with decreased gas exchange which then returns, in varying degree, towards normal. Our patients demonstrated sufficient abnormalities by x-ray films and short-term physiologic tests to indicate a significant exposure to chlorine.

Current treatment for pulmonary exposure to irritant gases, such as chlorine and phosgene, is based on the studies of Becklake et al who reported beneficial results from administration of ACTH (corticotropin) following pulmonary exposure to oxides of nitrogen. By analogy, this therapy has been extended to pulmonary injury caused by inhalation of other forms of irritant gas.

Factors involved in the outcome of pulmonary injury related to short-term sublethal exposure to chlorine gas include the intensity and duration of exposure, the presence or absence of preexisting cardiopulmonary disease, the time between exposure and treatment, the presence of secondary infection, cigarette consumption, individual variability in the inflammatory response, the presence or absence of prior long-term exposure to chlorine gas, and the type of treatment. In our patients, the majority of these factors were fortuitously controlled. The patients were siblings and might be expected to have reasonably similar responses to injury. Results of prolonged follow-up studies indicate that regardless of the variability of the individual capability for inflammatory response, exposure to chlorine gas in sublethal amounts in humans is capable of producing lasting abnormalities of pulmonary gas exchange. The difference in the treatment of the two patients suggests that therapy with adrenocortical steroids and oxygen may play a beneficial role in preventing these long-term changes.

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Adult-Onset Acid Maltase Deficiency*
Case Report of an Adult with Severe Respiratory Difficulty

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Pompe's disease (acid maltase deficiency) classically affects infants and children, with a few sporadic cases occurring in adults. An adult patient initially had progressive muscular weakness, exertional dyspnea, diaphragmatic paralysis, and objective evidence of restrictive respiratory disease. Muscle biopsy established the diagnosis of acid maltase deficiency. The patient's brother had died at the age of 44 years, after 23 years of a "progressive muscular dystrophy." Acid maltase deficiency should be considered in the differential diagnosis of progressive respiratory insufficiency associated with weakness.

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skeletal muscle, heart, liver, kidney, and cells of the central nervous system. Until recently, acid maltase deficiency was believed to be a disease fatal in early infancy. The babies would initially be short of breath, and chest x-ray films would show cardiac enlargement with congestive heart failure. The condition of the babies would follow a rapidly downhill course, and they would die from cardiorespiratory failure.¹

In 1968, Hudgson et al² reported a case of acid maltase deficiency presenting with weakness in adult life. Reports by Engel⁴ in 1970 and by Engel et al⁴ in 1973 provided details on seven patients with adult-onset acid maltase deficiency proven by muscle biopsy. The onset of weakness occurred in the third to the sixth decade of life. There was no family history of muscular disease in any of the cases. In each case, weakness was greater proximally than distally and greater in the pelvic than in the pectoral girdle. In three cases, there was respiratory muscular (intercostal and diaphragm) involvement. None of the patients had hepatic or cardiac enlargement.

The following patient has some unique features of acid maltase deficiency.

**CASE REPORT**

This was the fifth admission to Johns Hopkins Hospital for this 54-year-old black woman, who was admitted for evaluation of progressive muscular weakness of eight years’ duration.

**Family History**

The patient denied any knowledge of consanguinity in the family. The patient’s mother died at the age of 62 years from hepatic failure of unknown etiology. The patient’s father died of unknown causes at about the age of 40 years. Neither parent was known to have had any neuromuscular disorder. The patient had ten siblings, but only three survived childhood. Several died as infants, including a set of twins who died of unknown causes at the age of 18 months. One of the patient’s siblings who survived childhood developed a progressive muscular weakness at the age of 21 years. He was admitted to another hospital eight years later, where the diagnosis of “progressive muscular dystrophy” was made. He developed recurrent pneumonia and died at the age of 44 years.

**Past Medical History**

The patient’s general health had been good. She was admitted to the Johns Hopkins Hospital at the age of 31 years for thyrotoxicosis. This was treated medically for two years. The results of all subsequent tests of thyroid function had been normal. The patient was admitted for treatment of pneumonia at the ages of 33 and 51 years.

**Present Illness**

The patient was first seen in the neurology clinic of this hospital in 1968, complaining of difficulty in getting up from a sitting position. The problem had occurred for at least one year. The patient was also experiencing difficulty in climbing stairs and fell frequently when descending stairs. The results of studies of muscular enzymes at that time included an elevated concentration of creatine phosphokinase, aldolase, and lactic dehydrogenase. A biopsy of the left deltoid muscle revealed large intracellular vacuoles throughout the biopsy, without any inflammatory response. The biopsy was officially read as a “vacuolar myopathy.” Evaluations for possible malignant disease, collagen vascular disease, and thyroid disorder were within normal limits at that time. The patient was followed-up for the next six years, during which time she noted only gradually progressive weakness, which was maximal in her pelvic girdle. Two months prior to admission, the patient became unable to climb steps independently. For several years prior to admission, she also experienced progressive orthopnea, paroxysmal nocturnal dyspnea, and dyspnea on exertion and was treated in the cardiac clinic with digoxin and furosemide without much success. Because of progressive muscular weakness and shortness of breath, the patient was admitted to the neurology service for further evaluation.

**Physical Examination**

The patient was an alert, cooperative, slightly obese black woman who was sitting quietly, but who became dyspneic on assuming the supine position. Vital signs included blood pressure of 160/80 mm Hg, pulse rate of 90 beats per minute, and somewhat shallow respirations at a rate of 20/min. Her tongue was of normal size. Both diaphragms were elevated and moved poorly with effort. Cardiac examination revealed an apical impulse in the fourth to fifth intercostal space just lateral to the midclavicular line. The first and second heart sounds were normal; a grade 2/6 apical systolic murmur radiating to the axilla was noted. No third heart sound, rubs, or jugular venous distention was noted. The patient’s abdomen was obese without hepatomegaly. Neurologic examination revealed normal cranial nerve, sensory, and cerebellar findings. Muscle tone was normal. There was no muscular wasting. Testing of muscular strength revealed marked symmetric weakness in a limb-girdle distribution. Iliopsoas, hamstring, and gluteal muscles were most severely affected. Distal strength was quite intact. Deep tendon reflexes were symmetric and present throughout, although somewhat diminished in the lower extremities. No fasciculations were noted. The patient’s gait was waddling and somewhat wide-based. She was unable to perform heel, toe, and tandem walking.

**Laboratory Examination**

Laboratory findings included the following: potassium level, 4.3 mEq/L; bicarbonate level, 38 mEq/L; creatine phosphokinase level, 354 to 447 international units (IU)/ml (normal, less than 50 IU/ml); aldolase level, 12.8 units/ml (normal, less than 11 units/ml); serum glutamic-oxaloacetic transaminase, 38 to 44 units/ml (normal, less than 32 units/ml); rheumatoid factor, normal; antinuclear antibody titer, positive at 1:20; radioactive triiodothyronine uptake, 27 percent; and serum thyroxine iodine by radioimmunoassay, 11.2 µg/ml. Tests of pulmonary function revealed a restrictive defect with a forced vital capacity (FVC) of 1.56 L (55 percent of predicted) and a forced expiratory volume in one second of 80 percent of the FVC. The carbon monoxide diffusing capacity was slightly reduced at 8.8 ml/mm Hg/min (predicted, 11.1 ml/mm Hg/min). Analysis of arterial blood gas levels revealed a pH of 7.46, an arterial oxygen pressure of 59 mm Hg, and an arterial carbon dioxide tension of 50 mm Hg. A repeat muscle biopsy revealed intracellular vacuoles without inflammation. The
vacuoles stained positive with PAS. Histochemical analysis for acid maltase revealed 0.715 picomoles/min/gm of tissue (normal, 10.3 ± 1.0 picomoles/min/gm of tissue). Neutral maltase activity was 9.9 picomoles/min/gm of tissue (normal, 10.4 ± 1.5 picomoles/min/gm of tissue). The total muscle glycogen level was 1.2 percent (normal, 1.06 ± 0.23 percent). Echocardiographic studies revealed normal sized chambers but a slightly thickened left ventricular wall. The septum was somewhat dyskinetic, but the posterior wall moved well. An electrocardiogram revealed a shortened P-R interval.

For the past eight years, the chest x-ray film had been essentially unchanged. It demonstrated moderate elevation of both hemidiaphragms, bibasilar atelectasis or fibrosis, and a normal sized heart with a cardiothoracic ratio of 14/28 cm (Fig 1).

Fluoroscopic examination of the patient’s diaphragm eight years ago revealed severe limitation of the left hemidiaphragmatic excursion, with relatively normal excursion of the right hemidiaphragm. Recent repeat fluoroscopic examination revealed almost total paralysis of both hemidiaphragms.

**DISCUSSION**

Until recently, acid maltase deficiency was believed to be a congenital disease limited to the pediatric population. Sporadic cases are now being reported in adults, with the presenting complaint of muscular weakness. Very few of these patients developed any significant respiratory difficulty. In none of the cases was there any suggestion of familial involvement.

Our patient is unusual because in addition to her crippling muscular weakness, she has severe difficulty in breathing, primarily due to involvement of her respiratory muscles. This was clearly demonstrated by her chest fluoroscopic examination, which showed virtual paralysis of her hemidiaphragms, and by her pulmonary function tests, which suggested a restrictive pulmonary disease. In addition, the shortened P-R interval on the ECG may indicate myocardial involvement.

A unique feature of our case is the affliction and subsequent death of a sibling with a similar “progressive muscular dystrophy.” This raises the strong possibility that we are dealing with a familial type of adult-onset acid maltase deficiency.

Physicians should be aware of the existence of an adult form of acid maltase deficiency which may present with proximal muscular weakness and respiratory difficulty. One clue to the diagnosis is the inability of the patient to take a deep breath on multiple chest x-ray films and severe limitation of diaphragmatic excursion on chest fluoroscopic examination.

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