Short report

Myopathy due to juvenile acid maltase deficiency affecting exclusively the Type I fibres

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SUMMARY The clinical and laboratory findings of a patient with juvenile acid maltase deficiency are presented. The patient died from respiratory muscle weakness at age 31 years. Muscle biopsy shortly prior to his death showed remarkable vacuolation affecting exclusively type I fibres and mild myopathic changes of both types of muscle fibres, while the muscle biopsy at age 26 years had shown no evidence of acid maltase deficiency.

Hers¹ found that the disease which was originally described by Pompe² was due to deficiency of acid maltase, a lysosomal enzyme which hydrolyses both 1,4 and 1,6 α -glycosidic linkages. The invariably fatal infantile type² is characterised by cardiomegaly, hepatomegaly, macroglossia and flaccid weakness. Milder forms of acid maltase deficiency, presenting as myopathy, have been observed in children and adults³⁻⁶ and may be confused with muscular dystrophy or polymyositis. The biochemical basis for the different clinical manifestations of all these forms is obscure.

This report describes an unusual case of acid maltase deficiency.

Case report

A male physician, unmarried, had no neuromuscular disease or consanguinity in the family and both parents, one brother and two sisters were healthy. Early development was normal. The patient was never able to play or run like other children and he tired easily. At about age 6 years he had definite difficulty in going up, or down stairs, had difficulty with coughing and weakness of the arms. He had no problem with chewing or swallowing. He was never free of symptoms. There was no diurnal fluctuation. He became a physician and completed compulsory medical service in a rural general practice in Greece at age 25. At age 24 he was exempted from military service with a diagnosis of myopathy. At age 26 (1977) he was examined at the National Hospital for Nervous Diseases in London. There

was severe weakness and wasting of the sternomastoids; severe weakness of neck flexion; slight wasting of trapezii; wasting of shoulder and thigh muscles; severe weakness of triceps and finger extensors, brachioradialis and thenar muscles. All tendon reflexes were absent except the left ankle jerk. Cranial muscles and sensation were normal. The EMG showed changes consistent with myopathy. A left triceps biopsy showed some variation in muscle fibre size, with diameters from 30 to 120 μ m, slight proliferation of endomysial connective tissue, increase in subsarcolemmal nuclei, normal distribution of fibre types, and normal reactions for oxidative enzymes, phosphorylase and glycogen.

In May 1981 (age 31) he developed dyspnoea and was admitted to the Chest Hospital in Athens. Examination showed moderate weakness in the limbs, more proximally than distally, weakness of neck flexion and weakness of respiratory muscles. Apart from mild bilateral facial weakness and sternomastoid weakness cranial nerve findings were normal. Tendon reflexes and sensations were unchanged.

Normal data included blood count, ESR, blood sugar, serum creatinekinase and aldolase, ECG, chest radiography, edrophonium test and nerve conduction studies. The EMG showed primary myopathic changes. In a right biceps brachialis biopsy (paraffin sections: H&E, PTAH; cryostat sections; H&E, PAS, NADH, ATPase pH 9.4) all type I fibres had from one to four or more vacuoles (fig 1). A few fibres mainly type I, showed phagocytosis and necrosis or atrophy. Type II fibres had only trivial changes, mainly central nuclei. There was no inflammatory infiltration.

He was treated with prednisolone 30 mg on alternate days and he was sent to Newcastle-upon-Tyne in England for biochemical investigation. The needle biopsy which was carried out at the Newcastle General Hospital on the quadriceps muscle and together with the histological and biochemical studies established the diagnosis of acid maltase deficiency. There was a gross vacuolar myopathy and the vacuoles stained strongly with PAS. The acid maltase

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Table 1 *Acid maltase levels in muscle*

	Control	Patient	% Control
Acid glucosidase pH 4.0 nmol/min/g wet wt.			
Maltose	103.4	33.8	32.7
*MU & G	4.30	1.21	28.1
Neutral glucosidase pH 6.5 nmol/min/g wet wt.			
Maltose	40.5	74.6	184.2
MU & G	5.68	9.07	160
Ratio Acid/neutral activity			
Maltose	2.55	0.45	
MU & G	0.76	0.13	

*MU & G 4 methylumbelliferylDglucoside

level in muscle (see refs 2, 5 for method), was greatly decreased (Table 1), and urinary acid maltase activity (see refs 7, 8 for method), was also greatly decreased (Table 2). Neutral glucosidase activity was normal. Despite continued steroid therapy and a low carbohydrate diet, the respiratory difficulties increased, and he died of pneumonia and pneumothorax in Newcastle General Hospital at age 31. Necropsy was not permitted.

Discussion

Late-onset acid maltase deficiency may simulate muscular dystrophy or polymyositis^{8, 9} because of the

Table 2 *Acid maltase levels in urine*

	Control I	Control II	Patient	% Control I	% Control II
Acid glucosidase pH 4.0					
Maltose					
μmol/min/24 hr. sample	25.3		12.38	48.9	
nmol/min/mg creatinine	18		26.0	144.4	
MU & G					
μmol/min/24 hr. sample	1.38	1.50	0.65	49.8	43.4
nmol/min/mg creatinine	0.93	1.38	1.38	148	100
Neutral glucosidase pH 6.5					
Maltose					
μmol/min/24 hr. sample	9.23		19.66	213	
nmol/min/mg creatinine	6.5		41.66	641	
MU & G					
μmol/min/24 hr. sample	0.36	0.31	0.981	268.8	315.4
nmol/min/mg creatinine	0.26	0.26	2.08	800	727.3
Ratio Acid/neutral activity					
Maltose	2.74		0.63		
MU & G	3.64	4.82	0.665

Fig 1 *Transverse section from the right biceps brachialis. Note the remarkable vacuolation of type I fibres (dark fibres) (Cryostat Section, NADH). × 650*

proximal limb weakness and raised serum sarcoplasmic enzyme activity. An important differential sign is the disproportional involvement of the respiratory muscles.

Muscle biopsy may show only myopathic changes without any vacuoles¹¹ as in the first muscle biopsy of our patient at age 26. The histochemical PAS stain used to show the accumulation of glycogen may also be negative.¹¹ In juvenile and adult acid muscular deficiency muscle glycogen content varies from patient to patient and in the same patient from muscle to muscle^{3 13 14} but tends to be lower than in the infantile type and may actually be normal.^{6 8} In the childhood and adult types of the disease most vacuoles are found in type I fibres^{6 12 13} but they have never been exclusively confined to type I fibres as our case.

The present case report indicates that one cannot exclude acid maltase deficiency on the basis of a single biopsy and if the disease is suspected it would be necessary to carry out the appropriate biochemical estimations.

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