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Effect of enzyme replacement therapy (ERT) added to Home Mechanical Ventilation (HMV) in Adult Pompe disease

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Abstract

Adult Pompe disease/acid maltase deficiency is an autosomal recessive disorder resulting in accumulation of glycogen in skeletal muscles, leading to myopathy frequently involving respiratory muscles. This involvement can cause respiratory insufficiency that may present as acute hypercapnic respiratory failure. Enzyme replacement therapy (ERT) with alpha – glucosidase alfa, the only disease-specific treatment, has been available as treatment option since 2006. ERT has shown efficacy concerning muscle strength and pulmonary function in adult patients as well as positive association with survival. We present two cases where addition of ERT to Home Mechanical Ventilation (HMV) showed improvements in lung function and gas exchange that may not be entirely attributable to nocturnal HMV and therefore may further indicate the beneficial role of ERT in conjunction with HMV in Adult Pompe disease.

Introduction

Adult Pompe disease/acid maltase deficiency is an autosomal recessive disorder where deficiency of acid α-glucosidase (GAA) causes accumulation of glycogen in skeletal muscles, leading to myopathy frequently involving respiratory muscles that can cause respiratory insufficiency [1]. Disease-specific enzyme replacement therapy (ERT) has been available as treatment option since 2006. ERT has shown efficacy concerning muscle strength and pulmonary function as well as positive association with survival [2]. We present two cases where addition of ERT to Home Mechanical Ventilation (HMV) showed improvements in lung function and gas exchange which may not be entirely attributable to nocturnal HMV.

Case Report

Case 1

A 65-year-old office worker presented to a local hospital in 2005 with acute onset shortness of breath and was found to be in respiratory failure. He gave a history of two years of gradual onset fatigue, tiredness, and muscle weakness. A lifelong nonsmoker, he had no other past medical history. He was investigated for causes of respiratory failure and a muscle biopsy was done as suggested by neurologists that confirmed acid maltase deficiency. He was started on non-invasive ventilation (NIV) and as he was geographically relocated in 2007, we were asked to take over his care. On review in clinic, spirometry and blood gases were found to be stable with forced expiratory volume in 1 sec (FEV1) 1.07 L (liters), forced vital capacity (FVC) 2.02 L, partial pressure of carbon dioxide (PCO2) 6.6 kilopascals (kpa), PO2 9.0 kpa, and PH 7.38 on NIV, inspiratory positive airway pressure (IPAP) 12–22 cm of H2O and expiratory PAP (EPAP) 5 that was continued. He was also started on ERT. In 2008, he reported that his general weakness was much improved though he continued to feel breathless when lying down flat, probably reflective of an element of diaphragmatic weakness. There was also objective and subjective improvement with regards to his muscle function. In July 2008, he had a slight decrement in FVC with slightly high PCO2 of 6.54 kpa compared to the previous value of

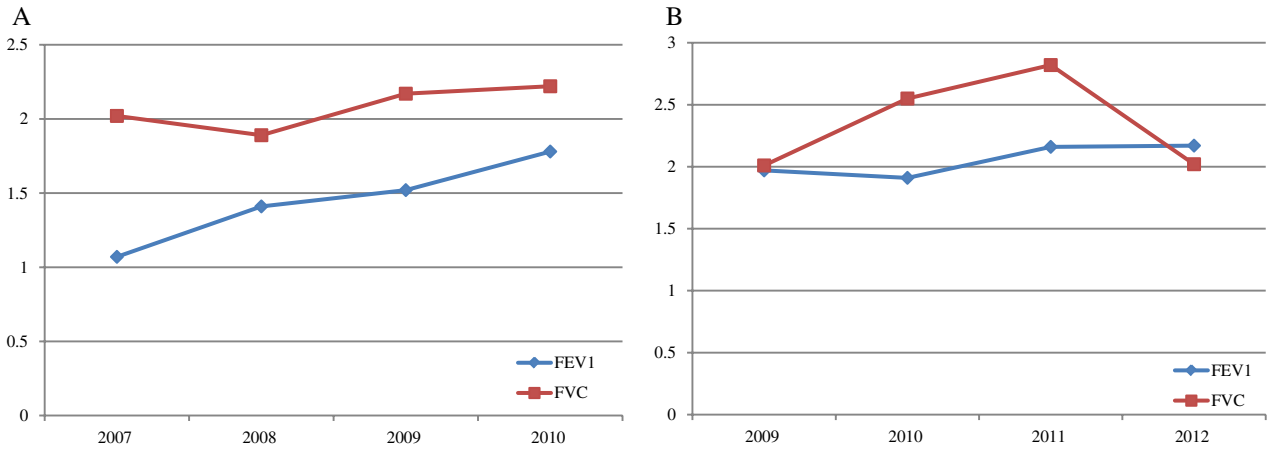

Figure 1. Lung function improvements with enzyme replacement therapy (ERT) added to Home Mechanical Ventilation (HMV) in Adult Pompe disease. A: Case 1: changes in FEV1 and FVC over 3 years. B: Case 2: changes in FEV1 and FVC over 3 years. FEV1: Forced expiratory volume in 1 sec, FVC: Forced vital capacity.

6.22 kpa. He, however, felt stable. On six-monthly review, he reported feeling very well with stronger voice and now could occasionally whistle. His spirometry also showed improvement (Fig. 1A). Mean expiratory pressure max remained the same around 86 cm of water. Significant improvement in his ventilation was demonstrated by increase in FEV1 of over 500 mL to 2.17 L. In September 2011, blood gas on air showed a normal PCO2. He has on-going follow-up with the respiratory department.

Case 2

A 63-year-old gentleman, a lorry driver by profession, presented in 2005 with cough, hoarseness of voice and shortness of breath. He was diagnosed with Pompe disease on muscle biopsy and started on NIV in 2008 for respiratory failure due to diaphragmatic weakness. His care was transferred to us in 2009 as he relocated. At that point his spirometry showed FEV1 1.97 L (67% predicted), FVC 2.61 L (62% predicted), at a ratio of 75%. His blood gases showed pH 7.39, PCO2 5.57 kpa, PO2 10.8 kpa, bicarbonate 25.1 mmol/L. He was changed to average volume-assured pressure support mode with IPAP 12–24 cm of H2O and EPAP 5 and started on ERT for Pompe disease at the same time. In July 2010 clinical follow-up showed identical spirometry with PCO2 5.9 kpa. We increased his tidal volume delivery to 750 mL. He reported symptomatic improvement and remained well. In October 2011, while on ERT and the same setting of NIV, he showed a much improved sniff nasal inspiratory pressure of 35 cm H2O from a previous value of 27 cm H2O in 2011. Spirometry was also better (Fig. 1B). With normal PH, pCO2 was 5.64 kpa. This was reflected in his improved mobility. In 2012, spirometry remained stable with pCO2 5.63 kpa on most recent review in 2014. He is under yearly follow-up at present.

Discussion

Pompe disease is a rare autosomal recessive disorder that usually manifests in childhood and is caused by deficiency of acid α-glucosidase [1]. Deficient activity of this enzyme causes intra-lysosomal accumulation of glycogen in skeletal muscle and other tissues. The phenotypic spectrum of the disease is broad but primarily presents in three forms: an infantile form in less than one year old with feeding and breathing difficulties with predominant cardiac involvement and an intermediate form which manifests with muscle weakness in childhood. Adult Pompe disease presents predominantly as a slowly progressive proximal myopathy due to reduced activity rather than absence of GAA. Diagnosis depends on patient history and physical examination findings, muscle biopsy, electromyography, and creatine kinase levels. Biochemical assay for enzyme activity is the method of definitive diagnosis [3] and may preclude the need for invasive muscle biopsy. Mutation analysis to confirm the presence of two mutated alleles can also be used. Although there is no cure yet, ERT has been highly effective at reducing clinical manifestations. In infants, ERT has been shown to improve overall survival, ventilator-free survival, cardiomyopathy, and motor development. With late onset Pompe disease, it causes disease stabilization with motor and pulmonary improvements [4]. Respiratory symptoms in Adult Pompe disease can be one of the first clinical manifestations of myopathy and usually precedes

limb muscular weakness. This can lead to respiratory insufficiency, sleep-disordered breathing, and eventual need for mechanical ventilation to prevent premature death from respiratory failure. We already know from large cohort series that long-term NIV produces a significant improvement in survival and quality of life in adults and children with stable chest wall and neuromuscular disease [5]. It reverses nocturnal hypoventilation, alleviates microatelectasis, improves sputum expectoration, and reduces the frequency of pulmonary infections. However as these cases demonstrate, there are potential additive benefits of ERT in patients on HMV. The improvements in lung mechanics and gas exchange may not be entirely attributable to nocturnal HMV and therefore may further indicate the beneficial role of ERT in Pompe disease, though this needs further evaluation.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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