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REVIEW

The role of respiratory management of Pompe disease

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Summary
Respiratory failure is an unavoidable event in the natural history of some neuromuscular diseases, while appearing very infrequently in others. In some cases, such as Pompe disease, respiratory failure progresses more rapidly than motor impairment, sometimes being the onset event. Home mechanical ventilation improves survival and quality of life of these patients, with a reduction in healthcare costs. Therefore, pulmonologists must improve their skills in order to play a more relevant role in the care of these patients. The aim of this statement is to provide pulmonologists with some simple information in order for them to fulfil their role of primary caregiver, enabling appropriate and rapid diagnosis and treatment.

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Contents

Introduction

The therapeutic approach to neuromuscular disease (NMD), including management of respiratory problems, has recently changed. Over the last decades, respiratory departments dealing with respiratory complications of NMD are increasing, facing the challenges of caring these complex patients. Nevertheless, a recent Italian survey showed that diagnosis, respiratory care, provision of information on respiratory complications and end of life decisions is still insufficient and needs to be improved.[1]

In this frame, Pompe disease has a specific relevance. The low prevalence of Pompe disease, prevents established experience and increases the risk of underestimating the severity of respiratory problems, with consequent therapeutic delays.[2] At difference with other NMD respiratory failure (RF) progresses more rapidly than motion deficit and defines the onset of the disease (Table 1).

This review does not add any new information to present knowledge but, due to the above need, aims to provide basic information to pulmonologists in order to improve their therapeutic role, and to perform a correct diagnosis and prompt treatment of Pompe Disease. In details the present experts' opinion claims the need to include always NMD (including Pompe disease) in evaluating symptoms, signs and functional results leading a patient to the pulmonologist.

Forms and characteristics of Pompe disease

Pompe disease, also referred to as acid maltase deficiency or glycogen storage disease type II, is a rare, progressive, autosomal recessive disorder caused by a genetic defect in acid α-glucosidase gene. This mutation is responsible for the lack of an enzyme called acid alpha-glucosidase (GAA). The GAA gene is highly pleomorphic; 289 sequence variations have been reported to date, including 197 proven pathogenic mutations.[3] Different mutations in the GAA gene are responsible for the large variability of onset age and disease severity. The lack of GAA, excessive amounts of lysosomal glycogen accumulate in the body leading to muscle damage including respiratory, with related clinical signs and symptoms of RF and skeletal muscle weakness. Overall incidence ranges from 1 in 33,000 to 1 in 300,000, depending on geographic region.[4] The clinical manifestations range from rapidly progressive early onset to slowly progressive late onset disease.[5] Classic early-onset Pompe disease more often presents in the first month of life with hypotonia, generalised muscle weakness, cardiomegaly and hypertrophic cardiomyopathy, feeding difficulties, failure to thrive, respiratory distress, and hearing loss. It commonly results in death in the first year of life from progressive left ventricular outflow obstruction. The non-classic variant of infantile-onset Pompe disease usually presents within the first year of life with motor problems and/or slowly progressive muscle weakness, typically resulting in death from ventilatory failure in early childhood. Cardiomegaly can occur, but heart disease is not a major source of morbidity. Late-onset (i.e., childhood, juvenile, and adult-onset) Pompe disease is characterised by proximal muscle weakness and RF without cardiac involvement. The onset can be as early as on the first or as late as on the sixth decade. On occasion the so called "juvenile-onset" or mild variant cases may present prior to 12 months. In late-onset form, the early manifestations are usually progressive muscle weakness and/or RF.[5] Independent of acute onset, progressive respiratory dysfunction develops in 70% of patients with a mean reduction in vital capacity (VC) ranging 0.9—4.5%.[4,6,7] Respiratory failure is usually cause of significant morbidity and mortality, the likelihood of needing mechanical ventilation (MV) increasing by an average of 8% each year following diagnosis.[5]