loumeral são dois exemplos de situações em que se pode avançar directamente para o estudo genético, evitando exames mais invasivos e até indutores de erro de diagnóstico, como é o caso da biópsia de músculo.

Apresentamos três casos clínicos cujo diagnóstico preciso só foi possível pelo concurso de uma equipa multidisciplinar experiente e trabalhando em permanente diálogo.

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NEW THERAPEUTIC APPROACHES IN ADULT NEUROMUSCULAR DISORDERS

Teresinha Evangelista, MD, PhD
The Newcastle University, John Walton Muscular Dystrophy Research Centre
Newcastle upon Tyne, UK
teresinha.evangelista@newcastle.ac.uk

Neuromuscular Disorders (NMD) comprise a diverse group of inherited and acquired disorders characterized by progressive muscle weakness and wasting. People of any age can be affected by NMD and clinical symptoms show a broad spectrum of severity. NMD often result in severe handicap of the patients. Pneumonia, cardiac arrhythmias, and cardiac and respiratory failure are the most frequent causes of death in NMD patients.

Over the past 20 years, research on NMD has undergone a revolution changing from a largely phenomenological science into a deeply analytical and technical field. Questions concerning the primary genes and basic mechanisms involved in NMD have been answered for a large number of conditions. This translated in better and earlier diagnosis, better counselling, and improvement of symptomatic treatments for the majority of NMD patients with significant gains in life quality and life expectancy. Unfortunately, cure or a near-normal life on treatment is rather the exception.

In recent years there has been an increase in novel therapeutic approaches from testing of existing and new drugs, to DNA delivery (anti-sense oligonucleotides and plasmid DNA), gene therapies and stem cells.

The use of viruses for the delivery of genes is now coming into clinical use. Safer vector designs based on adenovirus or lentivirus vectors have been developed and in 2012, a market approval of gene therapy was granted for the viral delivery of the lipoprotein lipase gene. For DMD, the challenge is the large size of the mRNA (14 kb) and the need to target all muscles. Thus dystrophin mini- or micro-genes have been designed and incorporated with muscle-specific promotors. Gene therapy is now coming of age for a whole range of different disorders. The application of exon skipping for the therapy of DMD depends on the identification of the precise mutation of the patient and the manipulation of the transcriptome. The correction of the reading frame in DMD patients should in many cases result in a BMD phenotype. Splice-modulation therapy aiming at correcting genetic defects by molecular manipulation of the pre-messenger RNA is a promising novel therapeutic approach for genetic diseases.