THE DIFFERENTIAL DIAGNOSTIC APPROACH TO LIMB GIRDLE WEAKNESS

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The term limb girdle muscular dystrophy (LGMD) includes a heterogeneous group of genetic disorders characterised by progressive muscle weakness and wasting involving mainly the pelvic, shoulder girdle and proximal limb muscles. The most frequent presentation is proximal weakness with onset in the second decade of life. However, a broadening phenotypic spectrum highlights the importance of considering LGMD as a differential diagnosis in almost any patient presenting with primary muscle weakness. Limb girdle weakness is a common feature in patients with dystrophinopathies, facioscapulohumeral muscular dystrophy, spinal muscular atrophy and many other forms of rare neuromuscular diseases. All of these diseases show a wider spectrum of clinical symptoms that can include cardiac and respiratory problems, joint contractures, and, in some childhood onset forms, general developmental delay. The most frequent age of onset for LGMD is in the second to third decade, but can vary from the first years of life up to the 5th decade of life. The genetic classification of LGMD has become increasingly complex over the years and even more so since the application of next generation sequencing technologies. Deep phenotyping, including muscle magnetic resonance imaging and comprehensive muscle biopsy analysis, is becoming more relevant with exome and genome sequencing, as the number of potentially pathogenic variants can be extremely high for an individual patient. A precise genetic diagnosis is critical, as it allows more accurate follow-up, the prevention of known possible complications, and appropriate genetic counselling for family members. As new therapeutic concepts are rapidly developing and first gene therapy trials have now started, making sure that patient are appropriately diagnosed is becoming more and more important.

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