Sarcoglycanopathies: A clinico-pathological study

There have been few publications relating to limb girdle muscular dystrophy (LGMD) in India. In this issue Meena et al describe clinical and pathological features of 26 LGMD patients from South India. The LGMDs are an expanding group of diverse conditions, the term LGMD was first introduced in 1954 by Natrass and Walton to describe a category of patients that did not fit into the recognized disorders of Duchenne, Becker and Facioscapulohumeral muscular dystrophies. Limb girdle muscular dystrophy is defined as a muscular dystrophy presenting with predominantly proximal weakness sparing facial, extraocular and distal muscles. Onset can be in childhood or adulthood but not infancy. Advances in molecular biology in recent years, have resulted in the emergence of distinct genetic entities and as a consequence a new numerical system of labeling was introduced by the European Neuromuscular Centre (ENMC). Autosomal dominant LGMD is designated LGMD 1A, 1B, 1C etc and autosomal recessive LGMD 2A, 2B, 2C etc; labeling is in the order of the identification of the genetic loci. To date there are seven dominant and 13 recessive forms, the latter being more common.

The sarcoglycanopathies (LGMD2 C, D, E and F) are a group of four genetically distinct but clinically similar muscular dystrophies. Each entity reflects the deficiency of a component of the complex of dystrophin-associated proteins. Onset is usually in childhood but can be later, the clinical picture is similar to Duchenne and Becker muscular dystrophy and affected females can be mistaken for manifesting carriers of DMD. There is often tongue and calf hypertrophy, scapular winging, cardiac and respiratory involvement is common. In Europe, the sarcoglycanopathies are relatively rare accounting for 5.6 cases per million in Italy and 25% of the ARLGMDs in the Netherlands. In their manuscript Meena et al describe the clinical and pathological features of 26 LGMD patients from South India, of which the sarcoglycanopathies were the most common group accounting for 54% of all cases. Furthermore, these Indian patients appear to have a milder phenotype with age of onset in the third and fourth decades compared with the European patients.

Genetic characterization for the ARLGMDs is not yet widely available around the world, but there may be clinical clues to aid the diagnosis. LGMD2A may present in the second decade with asymmetric pelvic weakness and early humeral involvement, there may be prominent muscle atrophy and early contractures but cardiomyopathy is rare. Muscle biopsy in LGMD2A demonstrates a dystrophic pattern with a propensity of lobulated fibers and there is reduced calpain on Western Blot analysis. LGMD2B is caused by mutations in the dysferlin gene. Onset is usually in late teenage years and may mimic acute myositis, the patient appearing normal prior to the onset. There is frequently weakness of the posterior peroneal compartment and, unusually for patients with pelvic girdle weakness, the patient cannot stand on his or her toes, the CK is very high. LGMD2I is probably the most common LGMD in the UK, the phenotype is similar to Becker muscular dystrophy, cardiomyopathy and respiratory involvement is frequent. Muscle biopsy shows a reduction in alpha dystroglycan and mutations are identified in the FKRP gene. A more severe congenital muscular dystrophy with central involvement (MDC1C) is allelic with mutations also occurring in the FKRP gene. Alpha dystroglycan is also reduced in muscle biopsies of patients with LGMD2K, however, learning difficulty may be an identifying feature of this entity. There is also a severe congenital form, Walker Warburg syndrome, with allelic mutations in the POMT1 gene.

It is very encouraging to see a developing interest in the muscular dystrophy field in India. In due course this will lead to improved diagnostic accuracy and improved management of the patients suffering with these conditions.

R. M. Quinlivan
Centre for Inherited Neuromuscular Disorders, Robert Jones and Agnes Hunt NHS Trust, Oswestry, UK.
E-mail: rcmq37@aol.com

References
