

## **NEUROMUSCULAR DISORDERS**

### **LIMB-GIRDLE MUSCULAR DYSTROPHIES**

The phenotype in limb-girdle muscular dystrophy (LGMD) type 21 was defined by mutation analysis, protein studies, and respiratory and cardiac involvement studied in 16 patients from 14 families with fukutin-related protein (FKRP) gene mutations and LGMD, at the Institute of Human Genetics, University Newcastle upon Tyne, UK. The age at onset ranged from 2 to 40 years (mean 19.2 years). Five patients had symptoms in childhood, including a peculiar gait, inability to run, muscle cramps, and myalgia. The remaining 11 patients had onset of symptoms in the 2<sup>nd</sup> to 4<sup>th</sup> decades. The predominant mode of presentation was a waddling gait, and difficulties in climbing stairs. Thirteen adults were homozygous for the common C826A mutation in FKRP. Three cases, 2 presenting in childhood with more progressive disease, were compound heterozygotes for C826A. Muscle involvement, including calf hypertrophy, was similar to dystrophinopathy, with proximal weakness. Patients with LGMD21 had cardiac complications (6 cases), and respiratory involvement, including the diaphragm (10 cases). Serum creatine kinase in all patients was 5 to 70 times normal. Muscle biopsies showed a reduction of the protein laminin  $\alpha 2$  immunolabeling. LGMD21 due to FKRP mutations is a common cause of LGMD, and patients frequently suffered respiratory and cardiac complications. (Poppe M, Cree L, Bourke J, et al. The phenotype of limb-girdle muscular dystrophy type 21. Neurology April (2 of 2) 2003;60:1246-1251). (Reprints: Professor Kate Bushby, Professor of Neuromuscular Genetics, Institute of Human Genetics, International Centre for Life, Central Parkway, Newcastle upon Tyne NE1 3BZ, UK).

COMMENT. Fifteen genetic subtypes of limb-girdle muscular dystrophy (LGMD) are recognized and identified by mutation analysis. Five are autosomal dominant and 10 autosomal recessive. LGMD21 is due to fukutin-related protein gene mutations and is a relatively common cause of LGMD. As indicated by Wicklund MP and Hilton-Jones D, in their editorial (Neurology April (2 of 2) 2003;60:1230-1231), early identification may diminish associated morbidity from respiratory and cardiac complications.

*Caveolin-3* gene mutations may cause the progressive LGMD type 1C and rippling muscle disease.

### **CAVEOLIN-3 MUTATIONS IN RIPPLING MUSCLE DISEASE**

Two unrelated patients with novel homozygous missense mutations (L86P and A92T) in caveolin-3 gene (CAV3), presenting with a severe form of rippling muscle disease (RMD), are reported from the University of Bonn, and other centers in Germany. Patient 1 had severe muscle stiffness from early childhood and contractures of the Achilles tendons. Patient 2 had slowly progressive muscle weakness beginning in early adulthood. Symptoms were restricted to skeletal muscles, and heart muscle was not affected. (Kubisch C, Schoser BGH, v Düring M, et al. Homozygous mutations in Caveolin-3 cause a severe form of rippling muscle disease. Ann Neurol April 2003;53:512-520). (Respond: Dr