

Clinical and Genetic Approach to Lipodystrophies

Bariş Akıncı

Dokuz Eylül University Faculty of Medicine, Department of Endocrinology, İzmir, Turkey

Lipodystrophies are a heterogeneous group of disorders characterized by a congenital or acquired loss of fat. Congenital generalized lipodystrophy (CGL) is characterized by near total absence of body fat at birth or in early infancy and the development of severe insulin resistance leading to poorly controlled diabetes. CGL is an autosomal recessive disorder. Several genes have been identified for CGL, which are 1-acylglycerol-3-phosphate O-acyltransferase 2, Berardinelli-Seip congenital lipodystrophy 2, caveolin 1, polymerase I and transcript release factor and c-fos. Familial partial lipodystrophy (FPL) is another rare genetic lipodystrophy syndrome characterized by the selective progressive loss of subcutaneous fat. Mostly, fat loss is observed in the arms and legs as well as in the chest and trunk regions. In some patients, subcutaneous fat may be accumulated in other areas of the body such as face and neck. FPL is associated with insulin-resistant diabetes, elevated triglyceride levels and fatty liver. Several genes have been identified for FPL, most of which are inherited as autosomal dominant traits that include lamin A/C (LMNA, Dunnigan variety), peroxisome proliferator-activated receptor gamma, perilipin 1 and V-akt murine thymoma viral oncogene homolog 2. A mutation in the cell death-inducing DFFA-like effector C gene causes autosomal recessive FPL that has only been reported in one individual

in the literature. Recently, mutations in the hormone sensitive lipase and phosphate cytidylyltransferase 1 alpha have been reported to be linked to partial lipodystrophies. Some FPL patients do not have mutations in any of these genes including those with FPL type 1 (Kobberling variety) suggesting that there should be additional genes to be identified. Some other rare genetic syndromes including mandibuloacral dysplasia, mandibular hypoplasia, deafness, progeroid features associated lipodystrophy syndrome, autoinflammatory lipodystrophy syndrome, short stature, hyperextensibility of joints and/or inguinal hernia, ocular depression, Reiger anomaly and teething delay syndrome, neonatal progeroid syndrome (Wiedemann-Rautenstrauch syndrome) and fibrillin 1 mutations have also been associated with various types of fat loss. In acquired lipodystrophies, patients develop fat loss at some point during life. They are not caused by genetic mutations. Fat loss is generalized in acquired generalized lipodystrophy, on the other hand, acquired partial lipodystrophy (APL) is characterized with fat loss on selective areas of the body that mostly starts at childhood. APL usually first affects the face, then progresses to neck, upper extremities, thorax and abdomen, sparing the lower extremities. The aim of this lecture is to cover both genetically based and acquired lipodystrophies and provide clinicians with a diagnostic algorithm on lipodystrophy syndromes. Potential therapies will also be discussed.

Key words: Lipodystrophies, clinical, genetic approach