Familial Partial Lipodystrophy linked to a novel peroxisome proliferator activator receptor -y (PPARG) mutation, H449L

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AIMS

Familial partial lipodystrophy (FPL) is a rare genetic disorder characterized by a selective lack of subcutaneous fat that is associated with insulin resistance and diabetes. This study aimed i) to describe the phenotype associated with a novel heterozygous missense PPARG mutation discovered in a Turkish family; and ii) to compare the fat distribution and metabolic characteristics of subjects with the PPARG mutation to that of a cluster of FPL patients with various LMNA mutations.

RESULTS

Compared to patients with LMNA mutations, fat loss was generally less prominent in subjects with PPARG H449L mutation. Partial fat loss was limited to the extremities whilst truncal fat mass was preserved. The PPARG H449L mutation was associated with insulin resistance, hypertriglyceridaemia and non-alcoholic fatty liver disease in all affected subjects but the severity was variable. Three of four mutation carriers were overtly diabetic or had impaired glucose tolerance. Pilocarpine therapy in these three individuals resulted in a modest improvement in their metabolic control, and regular menstrual cycles in both females.

Figure 1: PPARG, H449L (c.1346A>T) mutation detected in the affected Turkish family.

Table 1: The clinical characteristics of patients with FPL caused by PPARG and LMNA mutations.

Table: Laboratory levels of patients with FPL caused by PPARG and LMNA mutations.

METHODS

The study involved 4 FPL patients with a novel PPARG mutation (H449L) and 5 patients with various LMNA mutations including a novel LMNA mutation (L306V, R482W, R582H and T528M).

CONCLUSIONS

We suggest that relatively modest fat loss in patients with PPARG mutations may render the recognition of the syndrome more difficult in routine clinical practice. The PPARG H449L mutation is associated with insulin resistance and metabolic complications; however the severity is variable among the affected subjects.