**Table 1. Characteristics of patients investigated in this study**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Family D** | | **Family L** | **Family E** | | | **Family C** | | | **Mean ± SD** | **Median (range)** |
| **Patient number** | D-I2 | D-II3\* | L\* | E-I1 | E-II2\* | E-III1 | C-I2 | C-II1\* | C-II2 |  | |
| **Gender** | F | F | F | M | F | M | F | F | F |
| **Age (years)** | 54 | 24 | 67 | 69 | 40 | 17 | 41 | 17 | 13 | 38 ± 21.7 | 40 (13-69) |
| **BMI** | 23 | 25.5 | 22.7 | 25.7 | 30.7 | 23.8 | 29.8 | 25.4 | 19.6 | 25.1 ± 3.5 | 25.4 (19.6-30.7) |
| **Origin** | France | France | France | France | France | France | France | France | France |  | |
| **Age at diagnosis** | 54 | 15 | 40 | 58 | 38 | 17 | 41 | 15 | 13 | 32.3 ± 17.7 | 38 (13-58) |
| **Lipodystrophy** | Android habitus  Four limb lipoatrophy | Android habitus  Four limb lipoatrophy | Generalized lipoatrophy | Four limb, gluteal and trunk lipoatrophy  Cervico-facial fat accumulation | Lower limb and gluteal lipoatrophy | Mild lower limb, gluteal and trunk lipoatrophy | Android habitus  Four limb  and gluteal lipoatrophy  Cervico-facial fat accumulation | Android habitus  Lower limb  and gluteal lipoatrophy  Cervico-facial fat accumulation | Mild lower limb lipoatrophy |  | |
| **Acromegaloid features** | Present | Present | Present | Absent | Present | Present | Present | Present | Absent |
| **Muscular hypertrophy** | Present | Present | Present | Present | Present | Present | Present | Present | Not obvious |
| **Acanthosis nigricans** | Absent | Present | Absent | Absent | Present | Absent | Present | Present | Absent |
| **% of total fat (DEXA)** | 23.1 | NA | 12 | 16.4 | 21 | 13 | NA | NA | NA | 17.1 ± 4.9 | 16.4 (12-23.1) |
| **Serum leptin (ng/mL)** | 1.7 | 1.1 | 1.9 | 6.5 | 7.0 | 3.2 | NA | 12 | NA | 4.8 ± 3.9 | 3.2 (1.1-12) |
| **Glucose tolerance** | Gestational diabetes at age 20, 23 and 30  Permanent diabetes at age 34 | Impaired glucose tolerance  at age 15  Diabetes  at age 20 | Diabetes diagnosed at age 40 | Diabetes diagnosed at age 58 | Gestational diabetes  at age 30  Permanent diabetes  at age 38 | Normal glucose tolerance  with increased fasting insulin | Impaired fasting glucose  Antecedent of gestational diabetes | Diabetes diagnosed  at age 15 | Normal fasting glucose  with  increased fasting insulin |  | |
| **Serum fasting glucose (mmol/L) / insulin (pmol/L)** | 8 / NA  (insulin therapy)  Preserved  C-peptide  (1.2 nmol/l) | 6.1 / 402  at age 15  with BMI 24 | 3.9 / NA  (insulin therapy) | 8.3 / NA | 7.4 / 112 | 4.5 / 65.2 | 6.1 / 456 | 7.2 / NA  (insulin therapy)  High  C-peptide  (3.3 nmol/l) | 4.6 / 257 | 6.2 ± 1.6 /  258.4 ± 172.1 | 6.1 (3.9-8.3) /  257 (65.2-456) |
| **HbA1c** | 8 | 5.8 | 7.1 | 7.1 | 6.5 | 4.9 | 5.6 | 12.2 | 5.4 | 7.0 ± 2.2 | 6.5 (5.4-12.2) |
| **Triglycerides**  **( ≥ 2 mmol/L)** | Present | Present | Present | Present | Present  from age 18 | Present | Present | Present | Absent |  | |
| **Serum fasting**  **triglycerides**  **/ HDL-chol (mmol/L)** | 2 / 1.17 | 3.4 / 0.55 | 3.3 / 0.98 | 4.7 / 1.0 | 5.7 / 0.82 | 6.2 / 0.82 | 6.4 / 0.57 | 6.1 / NA | 0.5 / 0.98 | 4.3 ± 2.1 /  0.86 ± 0.22 | 4.7 (0.5-6.4) /  0.9 (0.55-1.17) |
| **Liver steatosis** | Present | Present | NA | NA | Present | NA | NA | Present | Present |  | |
| **AST / ALT (mIU/L)** | 18 / 29 | 50 / 78 | 45 / 63 | 22 / 38 | 24 / 23 | 19 / 10 | 30 / 56 | 171 / 216 | 36 / 36 | 46.1 ± 48.1 /  61 ± 61.8 | 30 (18-171) /  38 (10-216) |
| **Polycystic ovary syndrome (PCOS) or hirsutism** | Hirsutism  Oligo-menorrhea | PCOS | Absent | - | Mild hirsutism | - | PCOS | Oligo-menorrhea | Absent |  | |
| **Glucose and lipid lowering therapy** | Metf, Insulin  (> 2 U/kg/d)  Stat | Metf, iDPP4 | Metf,  Insulin  (> 3U/kg/d) | Metf, Sulf, GLP1R-A, Insulin | Metf, GLP1R-A, Stat | None | None | Metf,  GLP1R-A, Insulin | None |
| **Other signs** | Fatigue  Unexplained recurrent vomiting | Shoulder  Becker’s  naevus  Muscle Fatigability | High blood pressure  Myocardial infarction and rhythm disturbances | - | Severe fatigue  High blood pressure | - | - | - | - |
| ***PLIN1* variant** | c.1191\_1192del | | c.1191\_1192del | c.1202\_1205dup | | | c.1202\_1205dup | | |
| p.(Val398Glyfs\*166) | | p.(Val398Glyfs\*166) | p.(Pro403Argfs\*164) | | | p.(Pro403Argfs\*164) | | |

Patients numbers refer to Figure 1. Probands are depicted by an asterisk.

NA, not available; DEXA, dual energy X-ray absorptiometry; ALT, alanine transaminase; AST, aspartate transaminase; Metf, metformine; Sulf, hypoglycemic sulfamide; GLP1R-A, GLP1R agonist; iDPP4: dipeptidyl peptidase-4 inhibitors; Stat, statin.

The nomenclature of *PLIN1* variants is based on RefSeq accession numbers NM\_002666.5 and NP\_002657.3.