Familial partial lipodystrophy type 3 due to PPAR-gamma mutation: presentation with diabetes and severe hypertriglyceridemia

Joana Oliveira1,2,4, Filipe Cunha1,3,4, Elisabete Rodrigues1,3,4, Joana Menezes Nunes1,3,4, Ana Saavedra1,3,4, Ana Maria Manuel Costa1,3,4, Daniela Magalhães1,3,4, Rita Bettencourt-Silva1,3,4, Susana Fernandes1,4, João Paulo Oliveira1,2,3, Davide Carvalho1,3,4, Paula Fretas1,3,4
1Endocrinology, Diabetes and Metabolism Department, Centro Hospitalar São João; 2Department of Genetics, Centro Hospitalar São João; 3Faculty of Medicine, University of Porto; 4Institute for Innovation and Health Research, University of Porto - Porto, Portugal

Introduction: Familial partial lipodystrophy (FPL) is an autosomal dominant disease characterized by selective loss of subcutaneous fat from the extremities and gluteal region, with lipo hypertrophy of the face, neck and trunk. It is usually tightly linked with severe metabolic complications. FPL type 3 results from peroxisome proliferator-activated receptor gamma (PPAR-gamma) mutations.

53-year-old Caucasian woman

Endocrinology Department (04/10/2013)
Severe dyslipidemia - hypercholesterolemia and hypertriglyceridemia (11729 mg/dL) "Type 2" diabetes

Diabetes mellitus since she was 37 years old
*Diabetic nephropathy
Arterial hypertension
Nontoxic multinodular goiter
No history of pancreatitis or cardiovascular disease

Medication
Insulin detemir 52 units at breakfast + 52 units at bedtime
Insulin lispro: 8 units at breakfast + 8 units at lunch + 8 units at dinner
Vildaglutinmetformin 50/1000 mg twice daily
Simvastatin 20 mg once daily
Fenofibrate 267 mg once daily
Aspirin 100 mg once daily
Enalapril 20 mg once daily

Medical family history
Mother died at 55 years old from stroke (she had diabetes and dyslipidemia)
Father died at 85 years old from lung cancer
1 brother died at 31 years old from acute myocardial infarction
1 sister was diagnosed with a meningioma; 2 sisters had diabetes, arterial hypertension and dyslipidemia

Physical Examination
Weight: 50.3 kg | Height: 1.47 m | BMI: 23.3 kg/m²
Waist circumference: 80 cm
BP 150/85mmHg, HR 97bpm
No xanthomas, xanthelasmas or lipemia retinalis
Lipoprotein spectrophotometry with preserved subcutaneous fat in face and trunk

Laboratory tests
A1c 10.3%
Total cholesterol 921 mg/dL; HDL cholesterol 56 mg/dL; LDL cholesterol 195 mg/dL; triglycerides 4679 mg/dL; apolipoprotein B 99 mg/dL (53-138); lipoprotein(a) 4.3 mg/dL (<30)

AST 34 U/L (10-31); ALT < 3 U/L (10-31); GGT 40 U/L (7-32); ALP 83 U/L (30-120)
Creatinine 0.49 mg/dL (0.51-0.95)
Urinary albumin-to-creatinine ratio 108.4 mg/g

TSH 2.09IU/mL (0.35-4.94); T4L 1.00ng/dL (0.70-1.48)

Lipemic serum, with milky appearance

Variant c.581G>A (p.Arg194Trp) at exon 4 of the PPAR-gamma gene

Conclusions
The clinical features and biochemical profile suggested the diagnosis of genetic lipodystrophy, confirmed as FPL type 3. We underline the importance of clinical suspicion and early intervention of metabolic complications, in order to prevent early onset of cardiovascular disease and the occurrence of pancreatitis.