Severe insulin resistance and dyslipidaemia with unremarkable fat distribution in an adolescent girl due to mutation in the PPARG gene (Familial partial lipodystrophy type 3)

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Background

Mutations in the PPARG gene, encoding peroxisome proliferator-activated receptor-gamma (PPARG) are associated with Familial lipodystrophy type 3. PPARG regulates fatty acid storage and glucose metabolism.

The genes activated by PPARG stimulate lipid uptake and adipogenese by fat cells. In cases of lipodystrophy and defects of adipogenesis lipoid accumulates ectopically in the liver, skeletal muscle, pancreas and cardivoascular tissues and impairs the function of these tissues causing metabolic disease.

Patient

A 16 year old girl with a BMI on the 90th centile presented with severe insulin resistance, acanthosis nigricans and unremarkable fat distribution.

She was first treated with metformin and with a current HbA1c of 8.5 % started treatment with insulin glargin. Extensive hypertriglyceridaemia up to 5000 mg/dl [56 mmo/l] developed within 1.5 years treated by Omega-3-acids, MCT fat and fenofibrate. Transaminases were elevated and the liver was hyperechoic on the ultrasound. Father was healthy with triglycerids around 300 mg/dl.

An insulinresistance syndrome was suspected and a genetic analysis performed.

Method

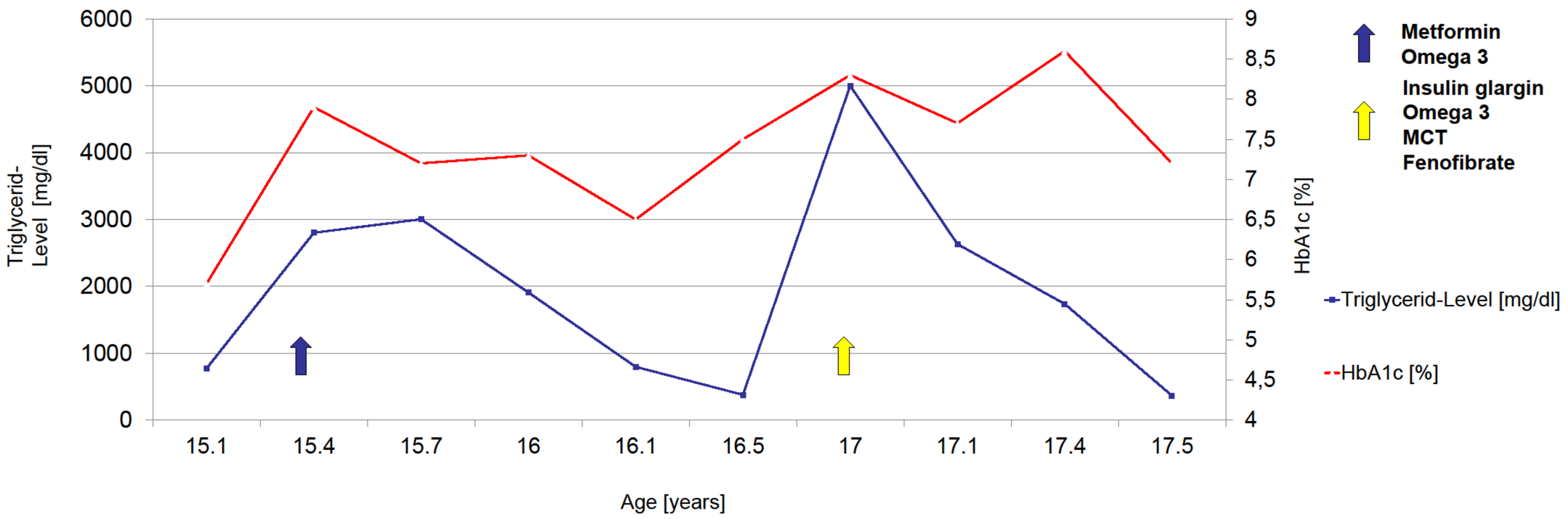
DNA from the patient has been screened for mutations in the PPARG gene by fluorescent sequence analysis and multiplex ligation dependent probe amplification (MLPA).

Results

A heterozygous sequence variant was found in the PPARG gene (c.609G>T in exon 3) as cause for the severe insulin resistance and dyslipidaemia.
The therapy is a low fat diet as well as pharmacotherapy.

Conclusions

Closely work up should be done if a severe metabolic syndrome is diagnosed without obesity in childhood or adolescence with extensive hypertriglyceridaemia regarding rare forms of lipodystrophy.



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