Control/Tracking Number: A-20-1580-EASD
Activity: Abstract
Current Date/Time: 3/22/2020 2:11:42 PM

A rare cause of type 2 diabetes mellitus, dyslipidaemia and pancreatitis: familial partial lipodystrophy. Presentation of a family with lipodystrophy

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Abstract:
Background and aims: Conditions of insulin resistance, hyperglycaemia and hypoglycaemia due to hyperinsulinaemia become more frequent and are sometimes hard to diagnose. Sometimes, rare conditions can be in the background. A 1983-born female patient presented at our outpatient department because of high glucose values and frequent hypoglycemic episodes. In the past medical history, she had a urogenital malformation operation at the age of 11. She was treated several times because of pancreatitis episodes between 2004-2012, in the background severe hypertriglyceridemia was present. In 2018, diabetes was diagnosed, along with severely elevated insulin levels. Dietetotherapy was initiated. Because of dyspnea, heart CT was undertaken, no coronary disease, but a highly enlarged liver of especially high density (16 HU) was seen. She could not take metformin because of abdominal complaints and subjective hypoglycemia-feelings, acarbose was also tried, but also led to more frequent hypos and abdominal complaints, thus only treated using diet, but no antidiabetics.
Materials and methods: Standard laboratory tests, abdominal MRI scan, skinfold measurements, estimation of total body fat content was performed using standard equations. Using blood samples, DNA-extraction and sequencing of the lamin-A gene has been performed.
Results: On physical examination, slightly Cushingoid face, trunk-localized obesity, absence of fat on the extremities, masculine-type musculature, expressed acanthosis nigricans were noted. Her HbA_{1c} value was 6.2, then 5.9%, the triglyceride value was 7.6 mM despite fibrate and ezetimib treatment, anti-GAD was negative, the C-peptide 4.9 ng/ml. ACTH, cortisol, renin-aldosterone, GH, IGF-1 did not indicate any pathology. Upon consultation with our endocrinologist, to exclude endocrine malignancies (like MEN-1), abdominal MRI was requested, that described a very large, highly steathotic liver (approx.. 35-40% fat content), signs of a chronic pancreatitis. The mother of our index patient showed a similar phenotype, she is known type 2 diabetic, currently treated with metformin and MDI insulin. The suspect of a genetic cause was strengthened by the phenotype of the sister of the index case, we initiated metformin. The distribution of body fat is rather uneven, skinfolds were: biceps: 4mm, triceps: 4mm, subscapular: 25 mm, suprailiacal: 9 mm, thigh: 6mm, calf: 6mm, waist circumference 86 cm, hip circumference 87 cm. The body fat content estimated from standard equations (depending on the equation, between 9.74%, 14.99% ill. 19.69%) markedly differed from the result of the bioimpedance-based value (26,2%), due to the uneven fat distribution. Upon permission of the ethical board, we turned to the European Lipodystrophy Register, beacuse of suspected familiar partial lipodystrophy. Genetic analysis was performed in Santiago de Compostela, and verified a heterozygous mutation at c.1445G>T, p.(Arg482Leu) in LMNA gene (exon 8), along with other, benign polymorphisms.

Conclusion: As a result of international collaboration, the proposed diagnosis has been verified. Work-up of other family-members is in progress.
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Keyword (Complete): 04 Monogenic forms of diabetes
Study information (Complete):
***Human studies**: Yes
***Animal Studies**: No

Grant Acknowledgement (Complete):
Please select Yes or No: No

Clinical Trial Registration Number (Complete):
: No
: N/A

Status: Complete