

Early diagnosis of type 2 diabetes in children with progeria syndromes



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INTRODUCTION

Progeria syndromes are rare in children and include several diseases which lead to premature aging mainly of the cardiovascular system early in childhood and adolescence. We report about 2 children in whom type 2 diabetes manifested at a very early age.

CASE 1

Boy with Cockayne syndrome, suffering from leucodystrophia, microcephaly, convulsions, severe psychomotor retardation and hepatopathy

Manifestation of diabetes at the age of 7 years with hyperglycemic-hyperosmolar coma: glucose 925 mg/dl, HbA1c 7.3 %, c-peptide 9 ng/ml, serum osmolality 345 mosm/kg, pH 7.4. Blood glucose was lowered slowly with small amounts of insulin and rehydration during several days.

Final therapy consisted of regular insulin administration to the feeding by percutaneous endoscopic gastrostomy. The boy deceased at the age of nine years.

CASE 2

Girl was known with Hutchinson-Gilford progeria syndrome, suffering from advanced cardiovascular aging with severe coronary arterial disease and hyporegenerative anemia with regular transfusions.

At the age of 14 years, routine blood test revealed a HbA1c of 8.6 % and a plasma glucose of 324 mg/dl. Together with elevated c-peptide (20,24 ng/ml) and insulin (500 mU/l) the diagnosis of type 2 diabetes was made.

As the girl had already received palliative care and after discussion with the parents, no specific treatment was started. She deceased at the age of seventeen years.

Cockayne-syndrome (CS)

CS is characterized by deficiency of the nucleotide excision repair system causes by variations in the genes for the proteins CSA und CSB (ERCC8, ERCC6). Main clinical features are microcephaly and growth failure, as well as progressive neurodegeneration, dermal photosensitivity with dry and crinkly skin, hearing loss and retinal dystrophia. Life span is about 6 years in the severe forms, but patients with mild forms may reach adulthood.

Disturbed glucose metabolism is reported in up to 15 % of patients, but insulin-dependent diabetes is rare in children and adolescents.

Hyperglycemic hyperosmolar coma is a rare manifestation of diabetes mellitus type 2 and is characterized by severe hyperglycemia and hyperosmolality with only mild acidosis. It might be complicated by multi-system organ failure with a high mortality already in adolescents.

Hutchinson-Gilford progeria syndrome (HCGS)

HGPS is caused by aberrant splicing of the LMNA gene resulting in the production of a disease-causing mutant lamin A protein called progerin. Main clinical features is severe premature atherosclerosis leading to death at about 13 years of age. Other symptoms include short stature, alopecia, reduced subcutaneous fat tissue and atrophic skin.

Hyperinsulinism and insulin resistance are common (50 % of patients) in contrast to fewer patients with disturbances in glucose metabolism during OGGT (20 %), and the diagnosis of diabetes is rare.

Recently several therapeutic strategies to alter progerin expression were reported. Experimental data show that treatment with metformin can alter the RNA-binding protein SRSF1 and via this pathway the formation of progerin. This might be a promising approach for patients with HCGS especially with insulin resistance syndrome.

CONCLUSIONS

Regular surveillance of glucose metabolism is warranted in children with progeria syndromes in order to detect early manifestation of insulin resistance and type 2 diabetes which is otherwise uncommon at this age in non-obese patients. Severe complications could occur if the diagnosis is delayed.

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