Phenotype and clinical course of diabetes mellitus in individuals with pancreatic hypoplasia due to a PTF1A enhancer mutation

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Background:
PTF1A mutations are known to be responsible for endocrine and exocrine pancreatic insufficiency due to a pancreas hypoplasia. The phenotypic variability of those cases even within the same family with the same mutation has been recently described.

Objective:
To describe the clinical course in three siblings with PTF1A enhancer mutations, in particular their anthropometric development, insulin requirement and diabetes control.

Method:
Retrospective analysis of growth, weight and BMI development as well as insulin requirement and HbA1c levels in these three children.

Results:
We report of three female siblings with a PTF1A enhancer mutation (g.23508437A>G), born to consanguineous parents. Age at onset of diabetes was at 10.6 and 7 years and at birth respectively; all exhibited pancreas hypoplasia leading to pancreatic exocrine insufficiency, requiring pancreatic enzyme substitution. Islet cell, insulin, GAD and IA2 antibodies were negative in all three children. However, transglutaminase antibodies were detected in the third sibling; duodenal biopsy confirmed a diagnosis of celiac disease.

Regarding anthropometry, birth parameters were as follows: BW-SDS: -3.09, -1.87 and -1.92, BL-SDS: -4.0, -0.17 and -1.77; current height at 10.5, 11.8 and 18.5 years: 146.8 cm (+0.37 SDS), 167,7 cm (+1.91 SDS), 165.7 cm (-0.38), corresponding BMI: 15,1 kg/m2 (-1.03), 18 kg/m2 (-0.06), 18,9 kg/m2 (-1.00).

Insulin therapy was started at diagnosis of IDDM. Average HbA1c levels at a current age of 10.5, 11.8 and 18.5 years were the 7.8%, 8.0% and 8.9% respectively, with a most recent requirement of insulin 0.5, 0.32 and 0.7 IU/kg body weight. Current pancreatic enzyme substitution therapy consists of pancreatin 2,000-3,000 IU/g fat/d.

Conclusion:
Subjects with PTF1A mutations seem to exhibit adequate anthropometric development and diabetes control under insulin and pancreatic enzyme substitution. Despite a non-immune etiology of IDDM, patients should be monitored for additional autoimmune disorders such as celiac disease, which can complicate the clinical course and affect diabetes control.