Neonatal Diabetes Caused by Pancreatic Agenesis

Which other genes should be used for diagnosis?

Permanent neonatal diabetes (PND) is an extremely rare condition. Few cases of PND caused by pancreas-development failure have been described, and only a few genetic causes have been identified so far (1).

We describe a boy with PND caused by pancreas agenesis, currently age 7 years. He is the first child of healthy, unrelated parents. He was born at 35 weeks of gestation, with severe intrauterine growth restriction (weight 1,620 g; length 45 cm). In the first day of life he developed severe hyperglycemia, and neonatal diabetes was diagnosed and treated with insulin, initially intravenously and then subcutaneously. Atrial septal defect was identified so far (1).

For diagnosis, DNA was extracted from whole blood samples from the patient. Several specific genes, such as KCNJ11, Sur1, GCK (involved in PND), Pdx1 (the key regulator of pancreas development and its promoter sequence upstream [E-Boxes]), Ptf1a, Sox9, Sox17, Hnf6, HlxB9 transcription factors expressed at the early stage, and HNF4a, as well as the NeuroD1, HNF1α, and HNF1β transcription factors expressed at the late stage of the pancreas differentiation, were amplified using specific primer by PCR and analyzed by direct sequencing.

The alignment of the screened gene to the human prototype sequences did not reveal any disease-causing mutations. Only a nonpathological insertion of two GCC triplets was found in the polyalanine stretch encoded in exon 1 of HlxB9. Thus, the patient has 16 instead of 14 alanine, with 11 encoded by the GCC repeat. The study by Ross et al. (5) did not find any pathogenic association related to the length of polyalanine stretch in the HlxB9 gene; we therefore considered this a polymorphism without disease relevance.

We add our case of PND caused by pancreatic agenesis to those already in the literature with normal Pdx1 and Ptf1a genes. Understanding the molecular network involved in the pancreatic development might provide the basis for the elaboration of new cell therapy approaches to treat diabetes (4).

References

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