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Novel GATA6-mutation in a boy with neonatal diabetes and diaphragmatic hernia. Review of the hereditary cases in the literature

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Introduction

Already in 1970 children with congenital heart defects and neonatal diabetes were described in whom subsequently a GATA6-defect was identified. Possible features of a GATA6-gene mutation are pancreas agenesis, neonatal diabetes, and congenital heart defect. Congenital hypothyroidism, hepatobiliary and gut abnormalities (gallbladder agenesis, biliary atresia) are described as well. Whereas the most cases are due to a de-novo-mutation, a few cases in the literature are described due to an inherited mutation.

Case

A term-born **boy**, small for gestational age, developed neonatal diabetes which resolved after five days of insulin supplementation. In addition, the boy presented with diaphragmatic hernia and a complex congenital heart defect (high grade stenosis of the left pulmonary artery, ventricular septal defect, persistent ductus arteriosus, atrial septal defect). At the age of one year, the boy presented with an early onset scoliosis. At the age of three years, a random evaluation revealed HbA1c 7.8% with no specific symptoms of diabetes. Autoantibodies to insulin, glutamic acid decarboxylase, beta islet cells and zinc transporter-8 were negative. Exocrine pancreatic insufficiency was excluded. Under insulin-therapy HbA1c is 6.2%.

His **mother** had a history of a complex congenital heart defect (atrial septal defect, ventricular septal defect, hypoplastic aortic arch, bicuspid aortic valve, stenosis of the right pulmonary artery, persistent ductus arteriosus) and had developed autoantibody-negative type-1-diabetes at the age of 25 years.

Underlying novel mutation in the boy and the mother:
Heterozygous GATA6-gene (c.1291C>T p.(Gln431*))

Comprehensive literature review

11 patients from the literature with hereditary cases of GATA6-mutation were identified. In all patients, onset of diabetes was earlier in the affected offspring. Congenital heart defects presented in the second generation with similar severity or aggravation of symptoms. In some cases, additional defects occurred in the second generation (e.g. diaphragmatic hernia, scoliosis, hypothyroidism).

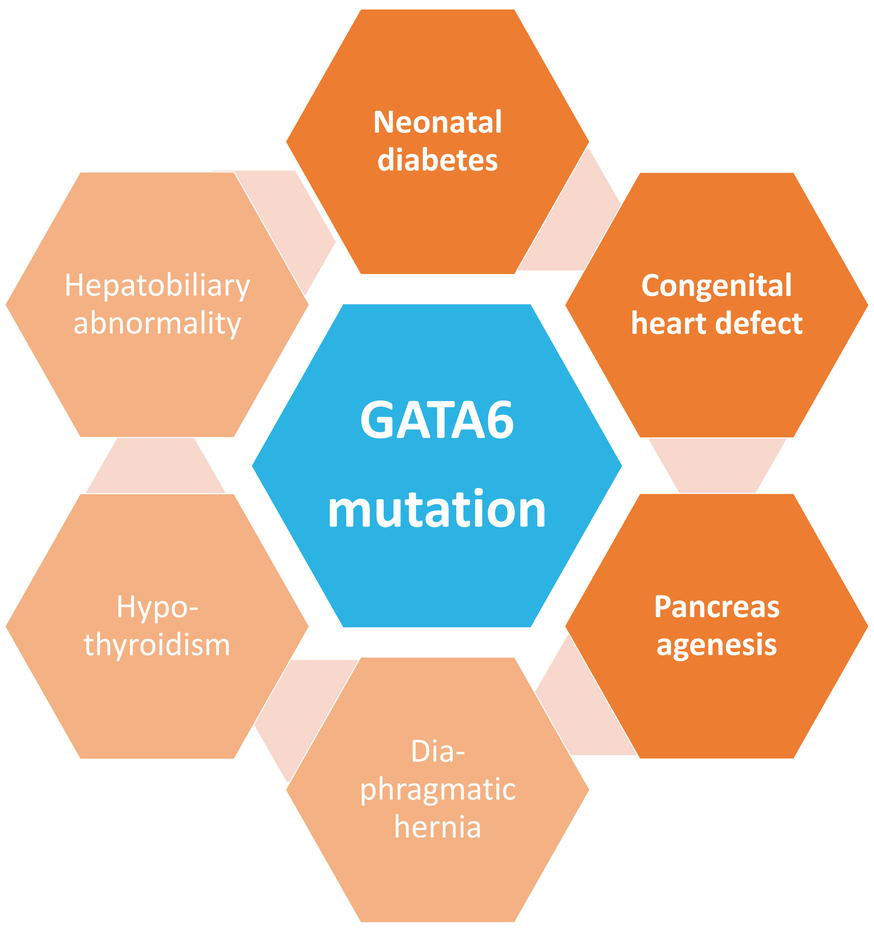

Figure 1. Possible phenotype of a GATA6-mutation.

Conclusion

Herein we present **a novel hereditary GATA6-mutation** (c.1291C>T p.(Gln431*)) in a boy with transient neonatal diabetes, diaphragmatic hernia, congenital heart defect and early onset scoliosis.

With these findings in our case and the compared hereditary cases in the literature we may postulate that **aggravation and anticipation** in hereditary GATA6-mutations seems to be a **constant phenomenon.**

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