DUOX2 Deficiency in Quebec: From Life-threatening Compressive Goiter in Infancy to Lifelong Euthyroidism

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TOPIC: Thyroid

CONTEXT
Congenital hypothyroidism caused by DUOX2 deficiency has a wide range of clinical presentations and phenotype-genotype correlations are not always straightforward1.

OBJECTIVES
To describe four children from Quebec with bi-allelic DUOX2 variants and widely variable phenotypes.

METHODS
Case series of four children seen at the endocrinology service of the Ste-Justine Hospital or the Centre Hospitalier de l’Université Laval for evaluation of thyroid function. Clinical and biochemical data were analyzed and molecular genetic studies were performed to document the etiology of thyroid dysfunction. In an attempt to explain the variability of their clinical presentation, exome sequencing targeting 12 other genes implicated in thyroid function was performed in all index cases.

RESULTS
Patient 1 is a 13 week-old boy who presented with a rapidly developing goiter resulting in severe tracheal compression and overt hypothyroidism of recent onset. Respiratory distress was successfully managed with levothyroxine replacement.

Patients 2 and 3 are siblings who harbor the same compound heterozygous mutations of DUOX2, yet presented with greatly discordant phenotypes: the sister had overt hypothyroidism at 14 months (TSH 93 mU/L, fT4 3.96 pmol/L) which evolved to mild hyperthyroproinemia at 15 years (TSH 7.22 mU/L, fT4 8.12 pmol/L), while the brother has lifelong euthyroidism.

CONCLUSIONS
Clinical expression of bi-allelic variants of DUOX2 is widely heterogeneous. Patient 1 is the first reported case of an infant with DUOX2 deficiency presenting with a compressive goiter with secondary respiratory distress, rapid diagnosis and medical treatment of which alleviated the need for surgery. Targeted exome study was not able to identify genetic modifiers of DUOX2 activity explaining the important inter and intra-pedigree phenotypic variability.

REFERENCES

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