Laron syndrome related to homozygous growth hormone receptor c.784>C mutation in a patient with hypoplastic pulmonary arteries

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Abstract

Laron syndrome, also known as growth hormone-insensitivity, is an autosomal recessive disorder characterised by short stature due to mutations or deletions in the growth hormone receptor (GHR), leading to congenital insulin-like growth factor 1 (IGF1) deficiency. Cardiac abnormalities, such as patent ductus arteriosus or peripheral vascular disease are rare in patients with Laron syndrome, but cardiac hypertrophy has been observed after IGF1 therapy. In this report, we present a 10-year-and-5-month-old girl with severe peripheral-type pulmonary artery hypoplasia and Laron syndrome related to homozygous GHR c.784>C mutation.

Keywords: Laron syndrome, hypoplasia, pulmonary arteries

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Laron syndrome, also known as growth hormone-insensitivity syndrome, is an autosomal recessive disorder characterised by short stature and caused by mutations or deletions in the growth hormone receptor (GHR), leading to congenital insulin-like growth factor 1 (IGF1) deficiency. Patients with Laron syndrome have low IGF1 levels despite normal or increased levels of growth hormone, and exogenous growth hormone does not induce an IGF1 response or restore normal growth, due to dysfunction of the GHR.

Clinical findings of Laron syndrome are short stature, delayed bone age, blue sclerae, hip degeneration, delayed bone maturation, and the absence of bone dysplasia and chronic diseases. Cardiac abnormalities are rare in patients with Laron syndrome, but cardiac hypertrophy may be seen after IGF1 therapy. In this report, we present a 10-year-and-5-month-old girl with severe peripheral-type pulmonary artery hypoplasia and Laron syndrome related to homozygous GHR c.784>C mutation.

Case report

A follow-up 10-year-old girl was admitted to our hospital's department of paediatric cardiology and paediatric endocrinology due to severe peripheral-type pulmonary artery hypoplasia and Laron syndrome. Her weight was 11.2 kg (<3rd percentile) and height was 88.2 cm (<3rd percentile). The patient’s age was 10 years and five months but her height was age two years and one month.

Physical examination revealed short stature, delayed pubertal signs, thrill at the suprasternal aspect, 4/6 systolic ejection-type murmur at the left upper sternal border and 3/6 systolic ejection murmur at the left lower sternal area. An ECG showed right-axis deviation and right ventricular hypertrophy. Echocardiographic examination showed right ventricular hypertrophy, tricuspid valve insufficiency and severe bilateral pulmonary artery hypoplasia. Right ventricular systolic pressure was calculated at 135 mmHg according to the tricuspid insufficiency.

From laboratory test results, the growth hormone level was >40 ng/ml (0.1–2.2) and IGF binding protein-3 (IGFBP-3) level was <0.500 µg/ml (1–10). Previously, IGF1 treatment had been given to the patient for three years (between ages four and seven) but her height remained below the third percentile (SDS –9 to –7.5). At the age of seven the growth hormone therapy was stopped.

Genetic analysis showed a homozygous GHR c.784>C mutation. Previously, the same mutation was detected by Akıncı et al. in a patient in our hospital and we realised that this patient was a relative of the one presented in this report.

Cardiac catheterisations four years earlier (Fig. 1) and at the age of 10 years (Fig. 2) revealed severe pulmonary artery hypoplasia. Right ventricular systolic pressure was measured at 122 mmHg and pulmonary artery pressure was 120/60–96 mmHg. The patient was deemed inoperable by the cardiovascular surgeons after the first cardiac catheterisation; however the second angiography showed the pulmonary arteries had improved slightly. Our surgeons therefore planned patch augmentation for the hypoplastic pulmonary arteries.
Laron syndrome, also known as growth hormone-insensitivity syndrome, is an autosomal recessive disorder that causes insensitivity to growth hormone and is characterised by short stature. It is associated with inadequate generation of IGF1 in response to growth hormone, due to dysfunction of the GHR. Laron syndrome is caused by diverse GHR gene mutations, including deletions, RNA processing defects, translational stop codons and missense codons. All the identified mutations involve the extracellular domain of the receptor and most are unique to families or geographic areas.1,3

Cardiac abnormalities are rare in patients with Laron syndrome, but cardiac hypertrophy may be seen after IGF1 therapy.4,5 In this report, we present a patient with Laron syndrome related to homozygous GHR c.784>C mutation, with hypoplastic pulmonary arteries and severe peripheral-type pulmonary stenosis. The second angiography showed that the pulmonary arteries had improved slightly. Our surgeons planned patch augmentation for the hypoplastic pulmonary arteries after the second cardiac catheterisation. We also detected a novel mutation in our patient. To the best of our knowledge, pulmonary hypoplasia and pulmonary stenosis have not been reported before in a patient with Laron syndrome.

Conclusion

Cardiac abnormalities such as patent ductus arteriosus or peripheral vascular disease are rare in patients with Laron syndrome, but cardiac hypertrophy has been observed after IGF1 therapy. Here we report on a 10-year-and-5-month-old girl with severe pulmonary artery hypoplasia and Laron syndrome related to homozygous GHR c.784>C mutation.

References