

IGF-1 deficiency: an important differential diagnosis in severe growth failure and its excellent response to rhIGF-1 replacement therapy

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Background

Insulin-like growth factor-1 (IGF-1) is the key effector peptide in the control of normal growth. IGF-1 deficiency in the presence of normal growth hormone (GH) is associated with growth failure. This may be caused by primary defects in the GH-IGF-1 axis or by conditions such as malnutrition or chronic inflammation. Severe Primary IGF-1 deficiency (height <-3 SD, serum IGF-1 <2.5th centile, GH normal) is a licensed indication for rhIGF-1 therapy. We report a patient with severe failure to thrive, short stature and unexplained IGF-1 deficiency who showed an excellent response to rhIGF-1 therapy.

Case

- 10 month old girl with severe failure to thrive (weight: 4.2kg, -7.95 SDS, length 60.1cm, -4.40 SDS).
- Born at 36 weeks gestation weighing 2.85 kg.
- Non-consanguineous Caucasian parents
- No dysmorphism, No microcephaly
- No recurrent infections
- Good caloric intake.
- Gross motor delay
- Russell-Silver syndrome, skeletal dysplasia, malabsorption and chronic illness were excluded.

Investigations

Glucagon stimulation	Peak GH 6.33 µg/l with a baseline of 1.51 µg/l.
IGF1	Persistently undetectable(<3.3nmol/l)
MRI Brain	Normal Pituitary
IGF-1 generation	IGF-1 undetectable(<3.3nmol/l) after daily GH (35µg/kg/day x 4). IGFBP-3 increased from 0.5 to 1.3mg/l(NR 0.5-2.9)
GH receptor mutation	Negative
Thyroid Function test, ACTH, Cortisol	Normal

- GH therapy resulted in severe diarrhoea with no increase in height velocity or IGF-1 level.
- Commenced on treatment with 120µg/kg twice daily of rhIGF-1.
- After two years of treatment, height improved from -4.40 to -1.48 SDS and weight from -7.95 to -0.94 SDS.
- Serum IGF-1 level normalised and age-appropriate motor milestones were achieved .
- Exome sequencing results are awaited.

Conclusion

This child with IGF-1 deficiency associated with severe failure to thrive of unknown aetiology has shown excellent linear and developmental responses to within-label use of rhIGF-1 therapy and continues to benefit from this treatment.

