Recombinant human Insulin-like Growth Factor 1 (rh IGF1) treatment of a case of leprechaunism : A two and a half year follow-up

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OBJECTIVES

Leprechaunism due to a mutation of both alleles of insulin receptor gene, is a most severe and precociously life-threatening condition, difficult to treat. In leprechaunism rhIGF1 may replace insulin through the insulin-like metabolic properties of its own receptor.

Objective: to evaluate the efficiency and safety of long-term, administration of rhIGF 1 in a severely affected child.

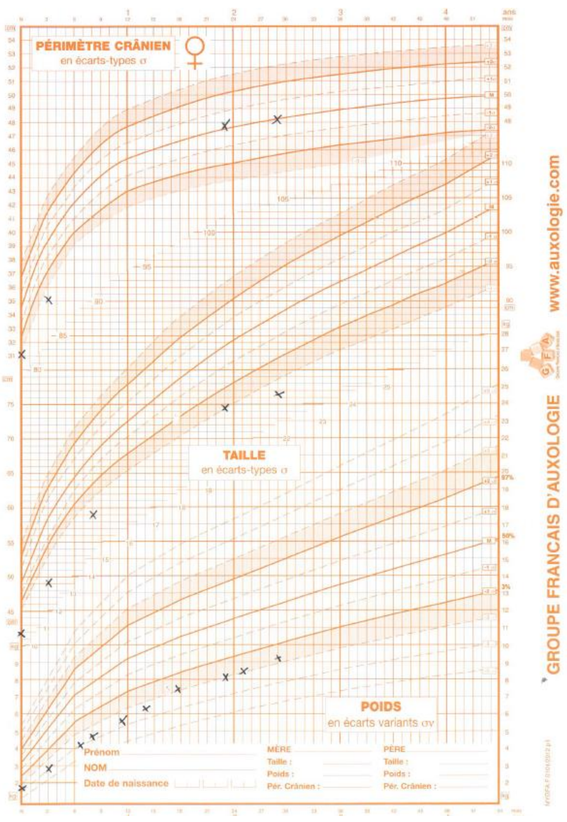


Figure 1 : Growth

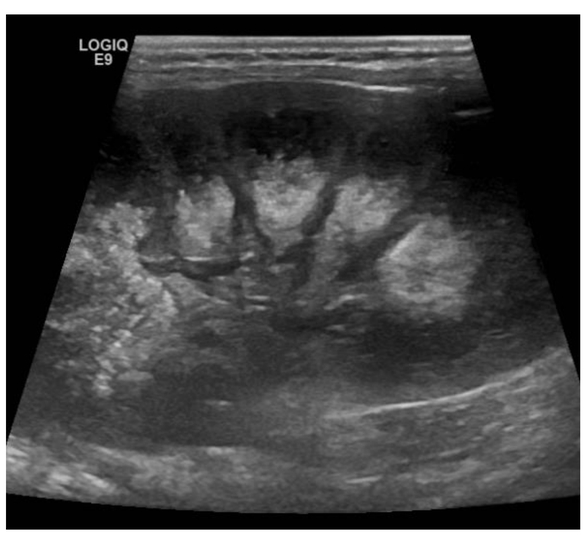


Figure 3 : ultrasound of left kidney

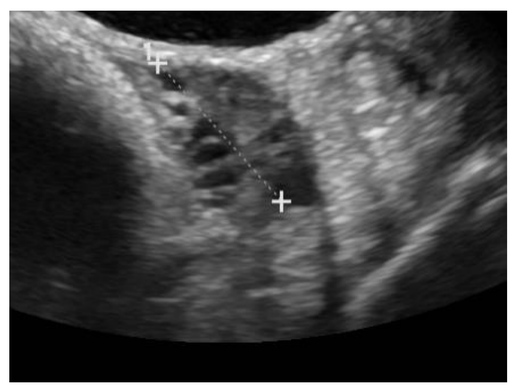
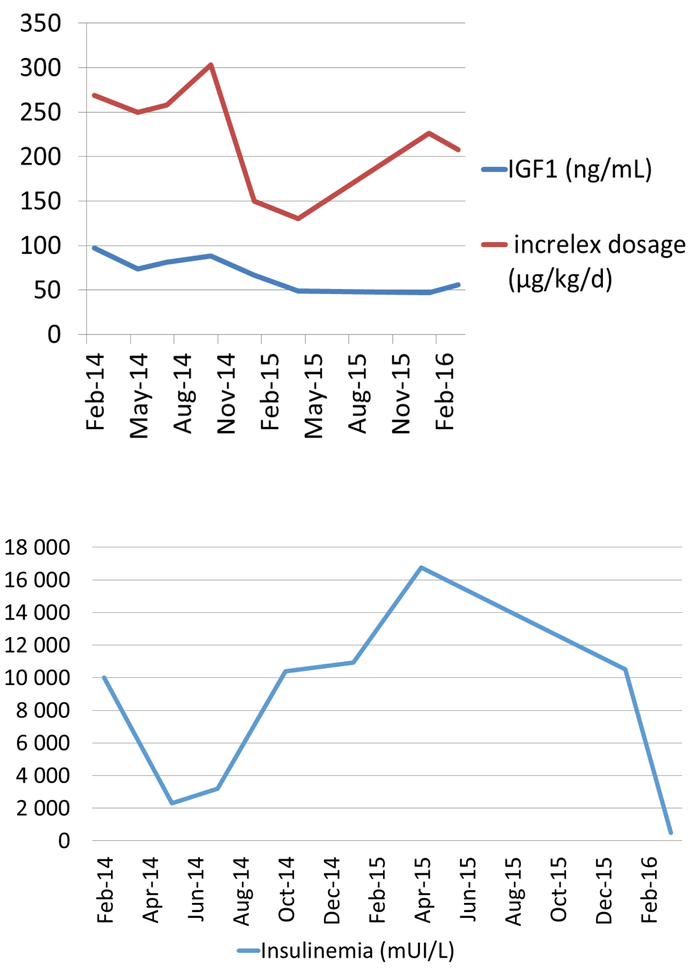


Figure 2 : ultrasound exam of left ovary



Figures 4 and 5 : Insulin and IgF1 levels. Increlex dosage

RESULTS

Case report: A first pregnancy of unrelated French Caucasian healthy parents was marked by a severe intrauterine growth retardation. All birth measurements at normal term were – 4 SDS. Immediately were noticed typical dysmorphic signs of leprechaunism.

The alternance of fasting intolerance, and of ketotic hyperglycaemia, became soon evident. Insulin and C-peptide levels were extraordinarily high, respectively 14 000 U/L and 30 ng/ml. IGF1 was undetectable in the plasma and leptin was present, 2.5 mg/L. She is heterozygous composite for mutations of the insulin receptor gene coding for V555D in the insulin binding domain, coming from her father and A1055V in the tyrosine kinase domain, coming from her mother. Under continuous enteral nutrition, metformin corrected hyperglycaemia but not hyperinsulinaemia. Extension investigations evidenced the persistence of growth retardation *(figure 1)*, hypotonia, hypertrophic cardiomyopathy, bulky multifollicular ovaries at US *(figure 2),* hyperandrogenism, hypercalciuria with low parathyroid hormone levels and nephrocalcinosis *(figure 3)*, treated by bisphosphonates.

rh IGF1 was continuously administered by a subcutaneous route through a pump from the age of four months and adjusted according to 2-3 SD plasma IGF1 levels from a 300 to 400 µg/kg/d. rhIGF1 administration medication allowed insulin levels to fall to 1000 U/L levels*(figures 4 and 5)* , without worsening of hyperglycaemia. Cardiomyopathy was contained with the help of a beta adrenergic blocking agent, lipoatrophy disappeared, leptin levels doubled, growth improved, ovary volume halved, hyperandrogenism vanished, but adenoids grew dramatically, needing several nasal curettages.

CONCLUSIONS

In leprechaunism, early rh IGF1 administration improves growth, adipogenesis, hyperinsulinaemia and ovarian hyperstimulation but adverse effects may occur, linked either to this medication or to the natural evolution of the condition.

REFERENCES

IGF-I treatment of insulin resistance
Anna McDonald (*European Journal of Endocrinology (2007) 157 S51–S56*)

55ESPE 193--P1

Diabetes

Jacques Weill

DOI: 10.3252/pso.eu.55ESPE.2016

Poster presented at: ESPE 2016 PARIS 10-12 SEPTEMBER