# Leptin replacement improves central ventilation in a patient with congenital leptin deficiency: first report in childhood.

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## Introduction

**Congenital leptin deficiency (CLD) is an autosomal recessive disorder characterized by severe early-onset obesity due to hyperphagia with food seeking behavior and impaired satiety. Body composition measurements show the preferential deposition of fat mass giving a distinct clinical appearance with excessive amounts of subcutaneous fat over the trunk and limbs. The impact of obesity in obstructive sleep apnoea hypopnoea syndrome (OSAHS) was originally reported as mechanical, but recent data suggest that adipokines may influence central ventilation. We highlight that treatment with recombinant human leptin (RHL) in CLD with OSAHS improves ventilation before weight loss.**

## Case Presentation

**A 10 months old female of Pakistani origin was referred to the Obesity Clinic of the Royal Hospital for Sick Children of Glasgow for severe obesity. At first clinical evaluation she presented weight of 15.85Kg (+5.55SDS), and BMI of 29.35 Kg/m2 (+5.25SDS) (Figure 1). She was born at term after an uneventful pregnancy, to consanguineous parents. No significant past medical history was referred. The mother reported a rapid weight gain during first months of life, due to intense hyperphagia with food-seeking behaviour. Family history revealed a first cousin with CLD: genetic analysis confirmed the same homozygous leptin mutation. RHL replacement was started at the dose of 0.06 ml twice daily, with good reduction of appetite immediately.**

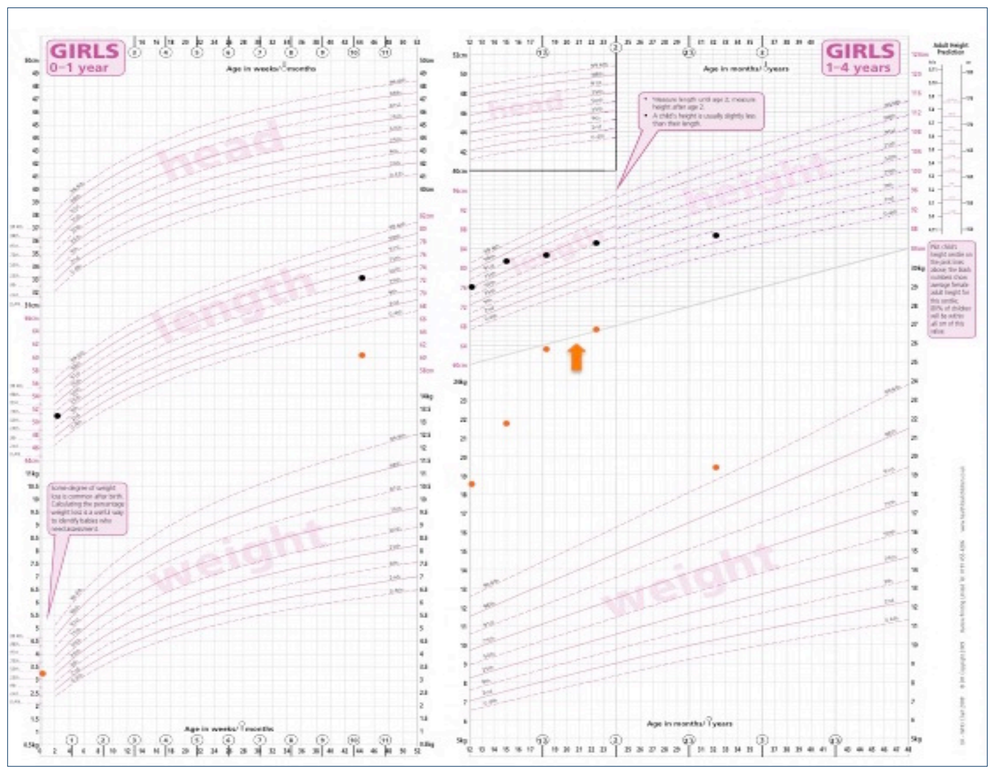


**Figure 1**: UK-WHO Growth chart for Female (0-4 years). Red spots represent the weight measurements, while black spots height evaluations. Red arrow indicates when RHL replacement was started

## Sleep Studies

**Oxicapnography was performed before starting treatment, showing normal mean saturations and CO2 but clusters of deep desaturations (Desaturation index (DI) 19.8/hr of ≥4%).**

**After 50 days of RHL treatment polysomnography was performed, showing a significant improvement in clusters of desaturation (DI 9.3/hr) and a mixed pattern of both obstructive and central events with an AHI of 13.7/hr. At this stage the weight was stable at 26.9 Kg (+6.7SDS) and the BMI was 34.8 Kg/m2 (+6.6SDS) (Fig.1).**

**After 11 months of treatment a significant loss of weight was seen, with weight of 19.62 Kg (+3.05 SDS) and BMI of 25.5 Kg/m2 (+4.5SDS). Repeat polysomnography showed marked improvement with a DI 4.2/hr.**

| | Oxicapnography before starting RLH replacement | Oxicapnography after 50 days of RLH replacement | Oxicapnography after 11 months of RLH replacement |
|---|---|---|---|
| Median Sat | 98.93 | 98.87 | 96.92 |
| Mean Sat | 99 | 99 | 97 |
| 5th/95th percentile | 96/100 | 98/100 | 96/98 |
| >5% | | | |
| Dips (0< Duration <180) | 137 | 46 | 24 |
| Dips/Hr | 17.05 | 6.03 | 3.01 |
| Mean Nadir | 88.77 | 90.61 | 90.96 |
| > 4% | | | |
| Dips (0< Duration <180) | 159 | 71 | 42 |
| Dips/Hr | 19.79 | 9.31 | 5.26 |
| Mean Nadir | 89.65 | 92.38 | 92.48 |
| > 3% | | | |
| Dips (0< Duration <180) | 210 | 120 | 82 |
| Dips/Hr | 26.14 | 15.74 | 10.26 |
| Mean Nadir | 91.20 | 94.06 | 93.82 |

## Conclusion

**To the best of our knowledge, this is the first report showing an improvement in ventilation, in a patient with CLD following treatment with RHL before significant weight loss. In mice, leptin microinjections into specific brain areas, are associated with increased pulmonary ventilation and enhanced bioelectrical activity of inspiratory muscles, suggesting that leptin may influence ventilation through direct effect on respiratory control centres. Leptin may have a central effect on ventilatory regulation, which needs to be explored further.**