

A not so "simple obesity"

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Introduction

Childhood obesity is the consequence of a complex interaction among several factors: environment, genetics, endocrine disorders, medications and other conditions. Genetic factors are described to be causal factors in up to 30-50% of overweight conditions.

Although polygenic obesity is by far the most commonly observed, several obesity related syndromes associated with single gene defects have been identified.

Case Report

A three years old girl referred to our Clinic with slightly increased TSH value (TSH 5.81 mcIU/ml, normal fT4) and excessive weight gain since she was 2 year old. Born at 36 weeks gestation, birth weight 1920 gr (7^ocentile). No anamnestic pathological features were referred.

Family history included obesity, rheumatoid arthritis, high blood pressure, a maternal spontaneous abortion at 15ws and T2MD.

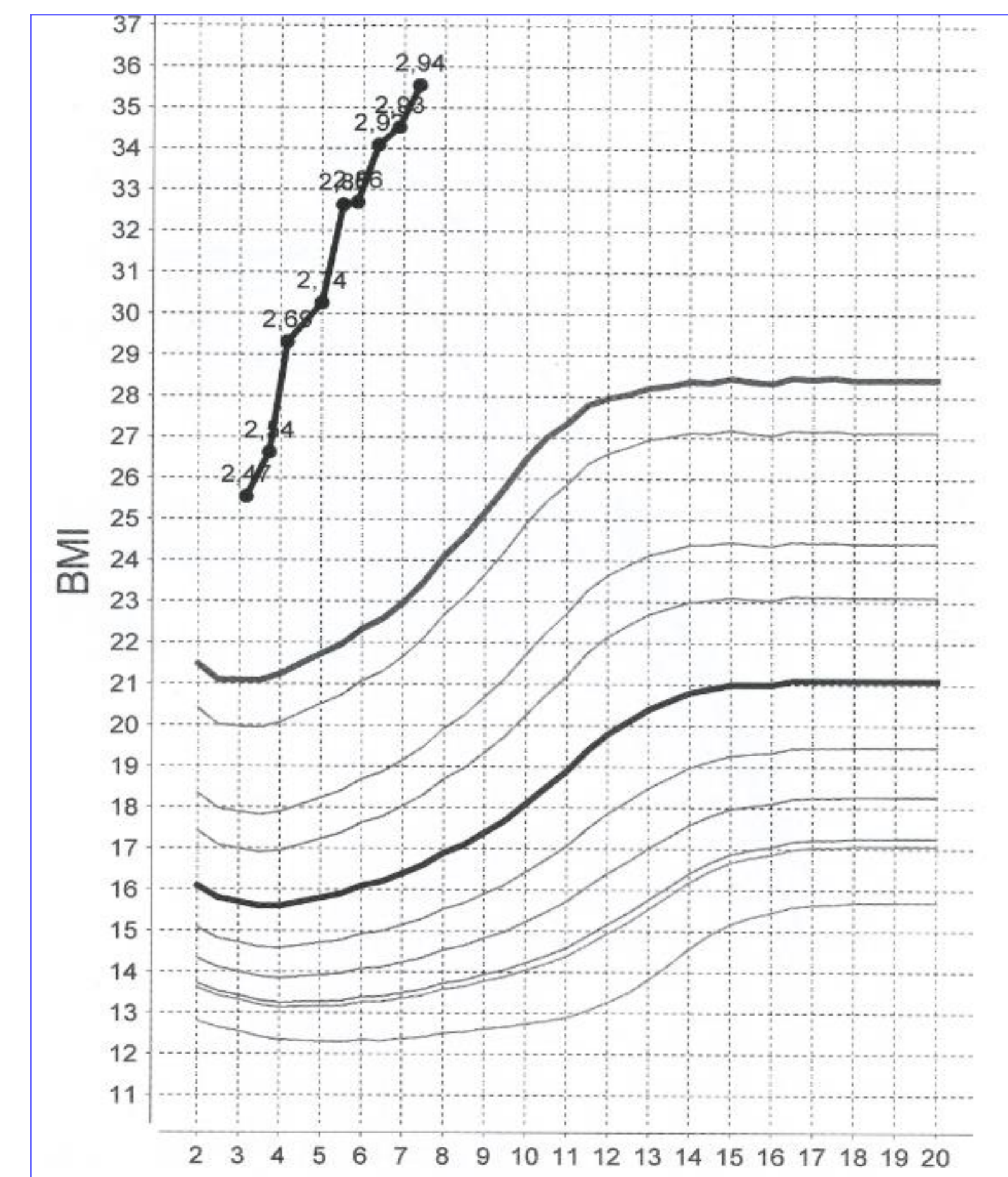
Our first clinical evaluation (at 3.1 years) revealed an important weight excess (BMI 25.6 Kg/m², SDS 2.47), flat feet, knock knees, pre-pubertal stages, no cognitive impairment or dysmorphic features.

Blood biochemical examinations showed:

- normal blood cells count
- normal liver and kidneys function
- insulin resistance (G/I 4.64, HOMA index 3.75)
- normal thyroid function (slightly increased TSH, normal fT4) and ultrasound examination
- pre-pubertal hormone levels
- normal adrenal secretion

Further investigations revealed:

- 46,XX karyotype
- negative brain MR
- liver steatosis at abdomen ultrasound
- pre-pubertal features at pelvic ultrasound



Methods

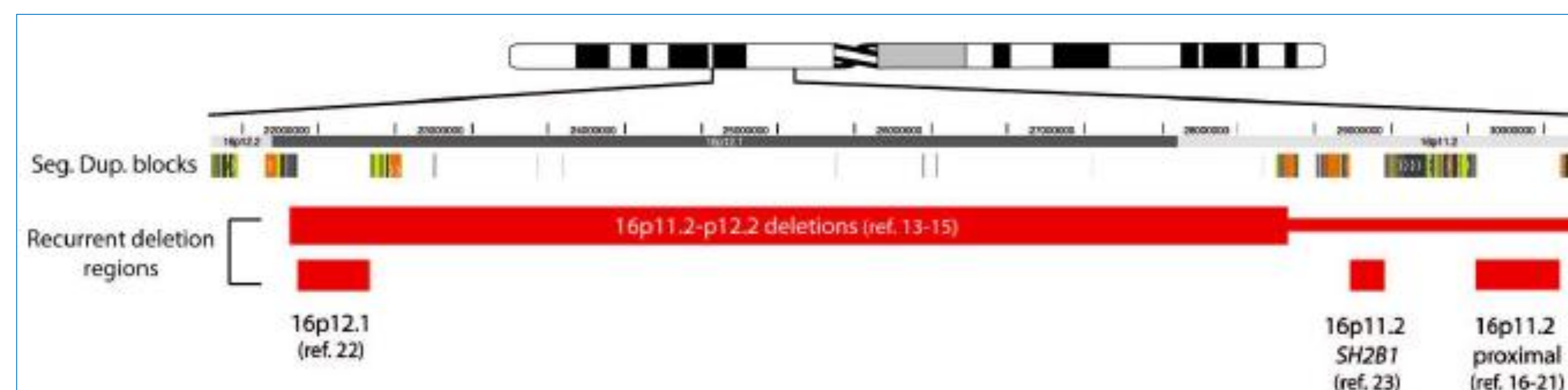
Once excluded main secondary obesity conditions, a dietetic program was started and she was evaluated every 6 months at our center

Because of weight increasing despite good compliance to dietary plan and physical activity program, we finally decided to attend CGHarray

Results

During dietary program patient's weight continued to increase (BMI 26.6 Kg/m², SDS 2.54 at 7 months of follow up; BMI 35.56 kg/m², SDS 2.94 at 4.2 years of follow up)

CGHarray revealed a heterozygous deletion of 232 kb (arr[hg19] 16p11.2(28,819,028-29,051,191)x1 in the 11.2 region of chromosome 16 p arm



Conclusion

Loss or gain of material from 16p11.2 is increasingly recognized as one of the most common structural chromosome disorders. The deletion identified in our patient involves 12 genes. The causative gene of obesity could be SH2B1 gene. This gene codes for SH2 adaptor protein 1 (SH2B1), involved in leptin and insulin signaling.

In literature, the loss of this protein is associated with a serious early onset obesity with insulin resistance. These features were observed in our patient.

In essential-like obesity not responding to dietary treatment, CGH array could be useful to improve diagnosis.

References: Bochukova EG. Large, rare chromosomal deletions associated with severe early onset obesity. *Nature* 2010

Bachmann-Gagescu R. Recurrent 200 Kb deletions of 16p11.2 that include the SH2B1 gene are associated with developmental delay and obesity. *Genetics in Medicine* 2010