Two unrelated cases of severe insulin resistance due to insulin receptor mutation discovered during adolescence


INTRODUCTION

Insulin resistance is most often found in obese patients with metabolic syndrome, and is considered as due to the excess fat mass. However, when the origin is genetic, the BMI is normal and it can be accompanied by acanthosis nigricans, hyperandrogenism and hyperinsulinism.

We report here two cases of insulin receptor mutation whose presenting signs were less noticeable.

Case report 1

• A 16-year-old girl (born eutrophic) consulted for hirsutism and secondary amenorrhea attributed to PCOS.
• No personal medical or surgical history.
• Familial background
  Multiple cases of hirsutism

Exam: 44.7 kg, 158.8 cm (BMI 17.7 kg/m²), axillary and inguinal acanthosis nigricans, mild acne, discreet hirsutism (Ferriman score 7), pubertal stage AAP454, no lipodystrophy.

• Biology:
  • Fasting glucose: 4 mmol/L
  • Fasting insulinemia: 170 µIU/L
  • OGTT was performed:
    • Testosterone Level 0.6 ng/ml (N < 0.5), AMH 23.95 ng/ml, 170HP normal
    • Pelvic ultrasound showed large ovaries of 9 and 8 cm² in favour of PCOS.

Pelvic ultrasound showed large ovaries of 10 and 8 cm² suggesting PCOS.

Examination of the family:

Overall: severe hyperinsulinism with normal BMI, PCOS and familial cases of PCOS

Suspected abnormality in the insulin signaling pathway: Insulin receptor gene analysis

• Heterozygote mutation of the INSR gene exon 17 (3164c>T), described in type A insulin resistance syndrome

Treatment: Metforming, improvement of hirsutism with acetate de cytoperone/estrogen

Case report 2

• A 13-year-old girl was referred for short stature (Height -2.5 SDS) with SGA (birth length 44 cm, at gestational age 41 weeks), no medical surgical history.
• Clinical examination was normal, pubertal stage was A2P353, 33.6 kg, 142.5 cm (BMI 17.2 kg/m²).
• Biology:
  • IGF1: 307 ng/ml
  • The glycemic nadir was 3.7 mmol/l (no hypoglycemia), and GH peak was 8 ng/ml during the insulin tolerance test (0.1 U/kg). All the investigations were normal, and the short stature was attributed to idiopathic SGA
  • At the age of 16, she was seen for acanthosis nigricans and primary amenorrhea. Pubertal stage was A4P454, and Ferriman score was 4, normal BMI, no lipodystrophy.
• Normal lipid profil and HBA1c

Overall: SGA without hypoglycemia during the insulin tolerance test, hyperinsulinism and PCOS with normal BMI