

Clinical case of a 10-year-old girl with papillomatosis due to severe insulin resistance type A

Elizaveta Orlova, Nadezhda Makazan, Alexandr Mayorov, Ekaterina Koksharova, Maria Kareva
Endocrinology Research Center, Moscow, Russia

BACKGROUND: Severe insulin resistance (IR) type A is a rare inherited disorder characterized by glucose metabolism disturbances without obesity, acanthosis nigricans and hyperandrogenia due to *INSR* defects.

CLINICAL CASE:

A 10-year-old girl was admitted because of skin **papillomatosis and hyperpigmentations** since her 7 yrs.

- Pubarche at 8 yrs, Telarche at 9 yrs.,
- Normal height and weight (SDS BMI +0.49),
- Acanthosis nigricans, no lipoatrophy,
- Puberty stage Tanner P3B3.

- **Insulin resistance and DM**

Table 1. Oral glucose test

Time (min)	0'	30'	60'	90'	120'
Glucose, mmol/l	3.0	6.6	7.8	9.5	11.4
Insulin, mU/ml	178	>1000	>1000	>1000	>1000

HOMA = 23.73 KARO = 0.02 (>0.3) MATSUDA 0.3 (>2.5)

HbA1C = 5.5%

Hyperinsulinemic euglycemic test (HET): M-value 1.22 mg | /kg/min

- **Hyperandrogenia**

- Testosterone 3.6 nmol/l (0.1 – 1.4)
- DHEA-S 7.6 mcmol/l (0.5 – 7.9)
- E2 106.4 pmol/l (50 – 120)
- LH 3.3 U/l (0 – 4)
- FSH 4.1 U/l (0.4 – 6.9)
- Bone age 11 yrs.
- Clitoromegaly
- Enlarged multifollicular ovaries (Right 5.5 ml, Left 5.2 ml)

Genetic analysis

Novel heterozygous p.E12228K mutation with uncertain pathogenicity in *INSR* was found.

Patient's father with the same mutation had multiple papillomas but normal glucose and insulin levels.

Treatment

Treatment with Metformin 2000 mg/day was started. After 3 months two-hours glucose level normalized (5.7 nmol/L), the level of IR decreased (M-value 2.11 mg/kg/min). The level of testosterone remained elevated (4.89 nmol/L) and volumes of ovaries increased (11.2 ml and 9.1 ml).

CONCLUSION:

Patients with acanthosis nigricans and papillomatosis should be investigated for IR. Severe IR is associated with signs of hyperandrogenism. Absence of IR in parent with the same mutation can be possibly explained by the penetrance. In our case of type A IR metformin normalized glucose metabolism but didn't treat hyperandrogenism.

