

# Heterozygous OTX2 deletion in a boy with normal eye development and normal pituitary function

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**Introduction.** *Orthodenticle homeobox 2* (OTX2) is a transcription factor that plays a critical role in forebrain and eye development. It likely interacts with HESX1 in Rathke's pouch and regulates various transcription factors as RX1, PAX6, LHX2. OTX2 heterozygous mutations or deletions lead to eye malformations such as anophthalmia, microphthalmia, coloboma, optic nerve hypoplasia but also dystrophy of the retinal pigmented epithelium (role in the mature retina) (Henderson and al), normal or hypoplastic pituitary gland and normal or ectopic posterior pituitary gland with isolated growth hormone deficiency or combined pituitary hormone deficiency (Diaczok and al). There is no genotype-phenotype correlation and variable presentation in the same family with whole gene deletion has already been described (Jones E and al).

## Case report:

A 3,2 year-old boy presented to our pediatric endocrinology unit for short stature.

## Neonatal history:

- born at term after an uneventful pregnancy with 3,010 kg and 50 cm

## Medical history:

- familial Mediterranean fever

## Familial history:

The mother's height is 156,3 cm and the father's height is 162 cm (target height 165 cm +/-8,5 cm (-1,7 SDS), Parents are non-consanguineous and healthy, Caucasians

## First examination

Height was 86,4 cm (-2,8 DS),

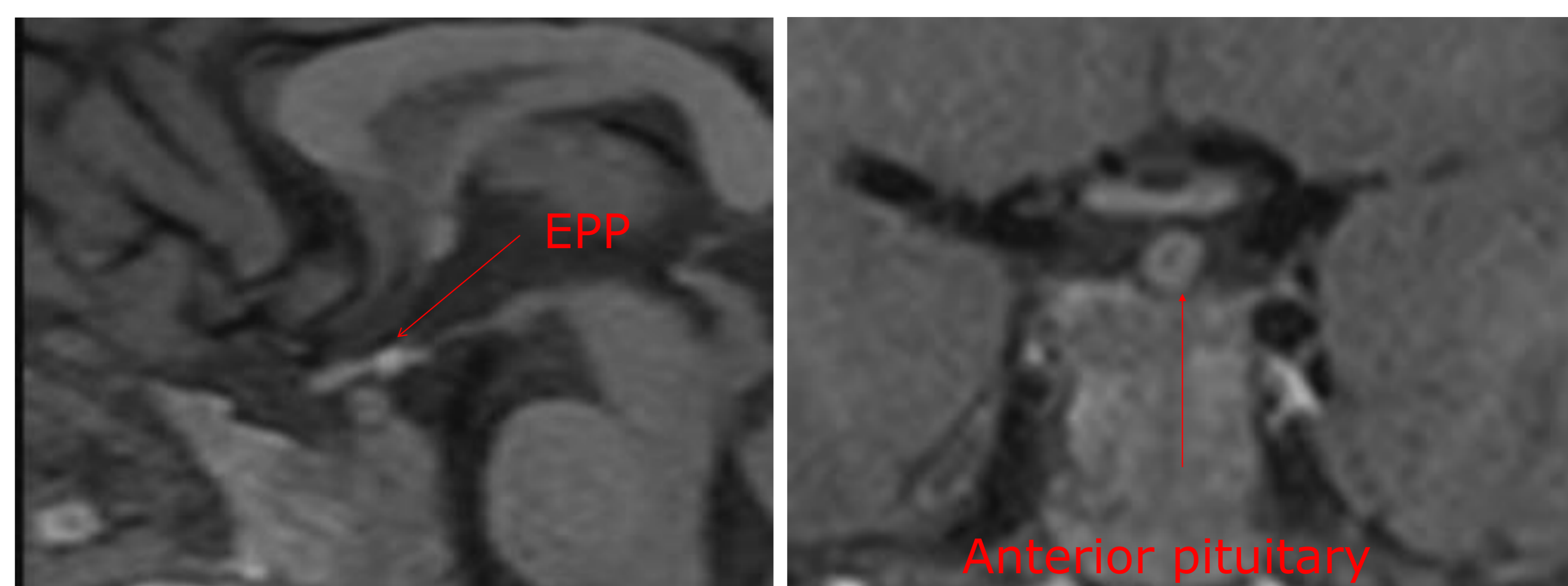
Weight 11,05 kg

Head circumference 46,8 cm (-3,4 DS).

No dysmorphic features. Tanner stage A1P1G1 with 2 ml testis bilaterally

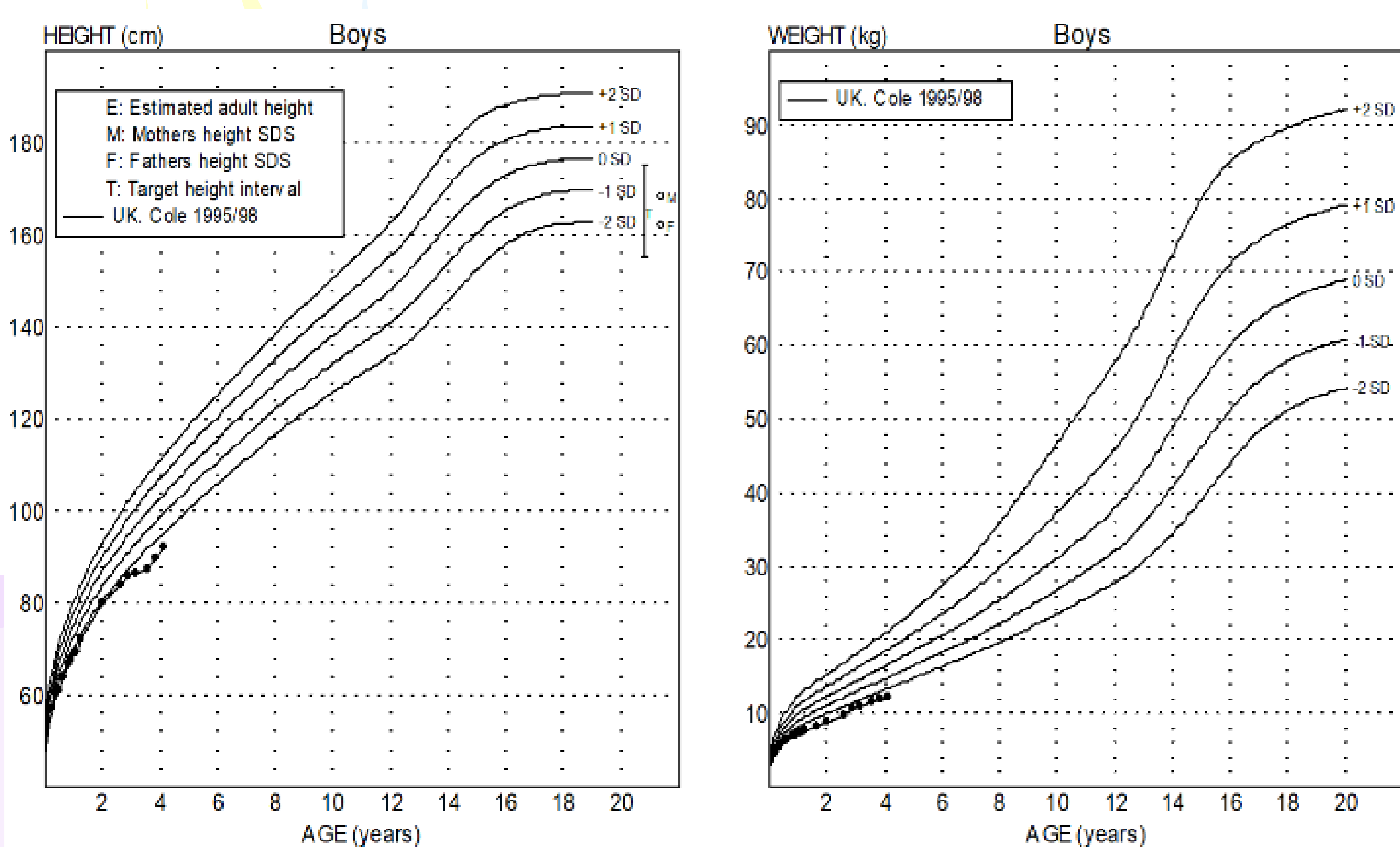
## Laboratory analysis:

- Normal thyroid function: free T4 18,6 pmol/l (reference range: 12,3-22,8)
- IGF1 normal for age : 67 ng/ml and 71 ng/ml (reference range: 15-200)
- insulin tolerance test showed a normal response for both growth hormone and cortisol : GH peak 7,44 ng/ml (normal value >7) and cortisol peak 561 nmol/l (normal value >550).
- Microarray analysis showed a heterozygous deletion of 14q22.3 including the whole OTX2 gene
- Both parents had normal microarray results



**Cerebral MRI** shows a malformation of the pituitary region, with an almost absent sella turcica, normal size but rounded anterior pituitary, with an ectopic posterior pituitary gland, thin pituitary stalk and no optic nerve abnormality.

**Extensive ophthalmological examination** showed no eye malformation or vision problem in our patient.



**In conclusion** we present on the case of a boy with heterozygous OTX2 deletion who harbors flat sella turcica, ectopic posterior pituitary but neither hormonal deficiencies so far nor eye malformation.

The anterior pituitary function will need to be followed-up as evolving hormonal deficiency is possible.

The retinal function will also need to be followed-up given the reported role of OTX2 not only in the developing, but also in the mature retina.

## References:

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