Isosexual precocity: uncommon presentation of a common disorder

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A 7-year-old girl presented with bilateral symmetrical enlargement of breasts of one year duration and one episode of vaginal bleed in August 1996. She did not have history of seizure disorder, meningitic or encephalitic illness, head injury or administration of oestrogen-containing preparations. She was an active child and had good scholastic performance.

On examination, her height was 108 cm (< 3rd centile), weight 21 kg (10–25th centile) and bone age was 3 years. Her pubertal status (Tanner) was B₃A₁P₁ (figure 1). She had no goitre and her deep tendon reflexes showed delayed relaxation.

Questions

- 1 What is the diagnosis?
- 2 What investigations would you perform next?
- 3 How would you treat this case?

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Figure 1 Photograph showing short child with premature breast enlargement (reproduced with the parents' permission)

Answers

QUESTION 1

The diagnosis is juvenile hypothyroidism presenting with isosexual precocious puberty.

QUESTION 2

Serum thyroxine (T_4), thyroid-stimulating hormone (TSH), prolactin and thyroid scan are required to establish the diagnosis. Her serum T_4 was 10 ng/ml (normal 60–120 ng/ml), TSH 50 μ U/ml (0.5–5 μ U/ml), prolactin 20 ng/ml (6–25 ng/ml) and ^{99m}Tc thyroid scan revealed a lingual thyroid (figure 2). As a lingual thyroid is smaller in mass, it fails to compensate for the increasing need of a growing child and results in hypothyroidism.

Figure 2 ^{99m}Tc thyroid scan showing tracer uptake in lingual region only

QUESTION 3

After confirmation of diagnosis she was put on thyroxine replacement therapy in gradually increasing doses (25–100 μ g). She had 'catch up' growth, regression of breasts and no recurrence of menses in 18 months of follow-up with normalisation of serum TSH (0.25 μ U/ml).

Discussion

Isosexual precocity is a rare monosymptomatic manifestation of juvenile hypothyroidism and other presenting features are summarised in box 1.¹ This was first described by Van Wyk-Grumbach in a series of three cases who presented with premature thelarche, galactorrhoea and menarche.² In this disorder the pubertal events are associated with decelerated growth and retarded bone age. The exact cause of precocity in hypothyroidism is not clear.

Monosymptomatic presentations of juvenile hypothyroidism

- short stature
- delayed puberty
- poor scholastic performance
- puberty menorrhagia
- isosexual precocity (Van Wyk-Grumbach syndrome)

Box 1

Learning points

- isosexual precocity is a monosymptomatic but rare presentation of juvenile hypothyroidism
- isosexual precocity with short stature and retarded bone age is a strong pointer towards diagnosis of thyroprivic hypothyroidism
- thyroxine therapy leads to complete arrest and regression of disorder

Box 2

Postulated mechanisms are 'specificity spill-over' which means positive feed-back effect of low serum thyroxine on pituitary gonadotropins as they are also glycoprotein hormones like TSH.² Hyperprolactinaemia,³ reduced gonadotropin clearance and decreased dopaminergic and opioid tone at the hypothalamo-pituitary axis⁴ are other plausible explanations. Elevated serum gonadotropins and oestradiol levels sometimes confuse the picture with gonadotropin-dependent precocious puberty (GDPP). However, this can be differentiated by the gonadotropin response to leutinising hormone releasing hormone (LHRH) which is present in GDPP but not in hypothyroidism-associated precocity.⁵ Our patient had normal prolactin (20 ng/ml) and elevated gonadotropins (leutinising hormone 6.5 IU/l, follicle-stimulating hormone 12.5 IU/l) and oestradiol (163 pmol/l) levels, however, her gonadotropin response to LHRH was prepubertal.

Thyroxine replacement therapy in optimal doses results in 'catch up' growth and complete arrest and regression of pubertal events.⁶

Final diagnosis

Juvenile thyroprivic hypothyroidism presenting as isosexual precocious puberty (Van Wyk-Grumbach syndrome).

Keywords: precocious puberty; juvenile hypothyroidism; lingual thyroid

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