

Case Reports

A case of partial androgen insensitivity syndrome (PAIS)

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Male pseudohermaphroditism is defined as incomplete masculinization of the external genitalia occurring in subjects with a normal male (46, XY) karyotype and with either testes or streak gonads¹. Resistance to the action of androgen is the most common cause of male pseudohermaphroditism. In this entity, the developing fetal testis secretes and converts testosterone to dihydrotestosterone normally but does not virilize the external genitalia because of the inability of the target tissue to respond to androgens². Approximately two thirds of cases of androgen insensitivity are familial with an X linked pattern of inheritance³.

Two phenotypic forms of the androgen insensitivity syndrome are recognised. The complete form (CAIS), also known as the testicular feminisation syndrome, is associated with normal female external genitalia⁴. CAIS may present in infancy or childhood with labial swellings or inguinal hernias that are found to contain testes. More typically, CAIS presents in late adolescence with primary amenorrhoea. The partial form of the androgen insensitivity syndrome (PAIS) is associated with a wide range of genital abnormalities and typically presents at birth with genital ambiguity. Severe hypospadias, micropenis, bifid scrotum and bilateral cryptorchidism are common. Alternatively, the external genital phenotype may be predominantly female with partial labial fusion and clitoromegaly⁵. Clinically milder forms of PAIS may also include isolated familial hypospadias and some cases of infertility in otherwise phenotypically normal males⁵.

The evidence to date indicates that a mutation of the androgen receptor gene is responsible for most if not all cases of CAIS. In contrast, many patients with PAIS demonstrate no defect in androgen binding and no androgen receptor gene mutation can be identified⁶.

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Case report

A 3 day old baby was admitted to the Lady Ridgeway Hospital in November, 1998 because the mother felt that the baby had a small penis. The baby, the product of a non consanguineous marriage, was a 3.2 kg full term infant. The pregnancy and delivery were normal. There was no history of jaundice, apnoeic attacks or convulsions. No hormonal treatment had been given during the antenatal period. There was no family history of a similar disorder.

The weight, length and head circumference were normal. There were no dysmorphic features and no midline facial defects. The stretched length of the penis was 1.5 cm. The urethral opening was located on the dorsum of the penis. Both testes were palpable in the scrotum and were normal in size. The cardiovascular, respiratory and central nervous systems were normal.

The random blood sugar was 3.9mmol/l. The serum electrolytes were as follows: sodium 138mmol/l, potassium 6.2mmol/l, chloride 92mmol/l. The blood urea was 3.6mmol/l. The bone age was normal. The serum thyroxine was 15.3mcg/dl on the sixth day after birth (normal range 4-16 mcg/dl). The serum TSH was 7.1mu/l on the sixth day after birth (normal range 3-18mu/l). The random serum cortisol level was 34nmol/l (normal 23-662nmol/l).

The serum testosterone was 740pg/ml on the ninth day after birth (normal range day 1-16 after birth 1.5-31 pg/ml). The urinary 17 ketosteroid level on the 12th day after birth was 17 mg/24 hrs (normal < 1 mg/24 hrs). The serum luteinizing hormone (LH) level was 2.2u/l (normal 1-2 u/l). The follicle-stimulating hormone (FSH) level was 2.4u/l (normal < 1 u/l).

A karyotype of peripheral leucocytes showed a 46, XY chromosomal pattern. A pelvic ultrasound study showed no vagina, cervix or uterus. An ultrasound scan of the abdomen showed no adrenal masses.

The baby was treated with 3 intramuscular injections of depot testosterone (25 mg) at monthly intervals.

The baby was readmitted to the ward at 2 years and 5 months of age for review. The stretched length of the penis was now 3 cm. The growth parameters were normal.

Discussion

The mean penile length for a full term baby is 3.5 cm with a standard deviation of 0.5 cm⁷. In micropenis the length of the penis is more than two standard deviations below the mean⁷. In our patient micropenis was present as the length of the stretched penis was 1.5 cm. The fact that the penile length increased to 3.0 cm following injection of depot testosterone suggests that further virilisation will occur at the time of puberty either as a result of endogenous androgen secretion or further testosterone therapy.

The markedly elevated serum testosterone level, the high urinary 17 ketosteroid level, the elevated LH and FSH levels together with increase in penile length after administration of testosterone established the diagnosis of partial androgen insensitivity syndrome (PAIS).

Although the term PAIS implies that virilisation will not occur in the long term, this may not be the case, even when there is a mutation of the androgen receptor gene⁸.

References

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