CASE REPORT

An unusual case of secondary amenorrhoea

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SUMMARY

A 22-year-old married woman presented with complaints of amenorrhoea and masculinisation. She had hoarseness of voice, hirsutism and ambiguous genitalia. Uterus, cervix and vagina were normal. Investigations revealed a high testosterone level, insignificant luteinizing hormone/follicle stimulating hormone (LH/FSH) and a raised 17-OH progesterone level. Ultrasonography revealed no ovarian or adrenal mass. A diagnosis of 21-hydroxylase deficient classic congenital adrenal hyperplasia, simple virilising form was considered. She was put on prednisolone and given oral contraceptive pill containing cyproterone acetate. Her testosterone level decreased and spontaneous menstruation started. She desired conception and ovulation was induced with clomiphene citrate. She conceived in the second menstrual cycle on clomiphene 50 mg. Imaging at 6 weeks revealed a viable fetus, and an anomaly scan at 16 weeks showed a healthy fetus. However, unfortunately, she aborted around 21 weeks. A scan immediately prior to abortion revealed a subchorionic haematoma.

BACKGROUND

Classic adrenal hyperplasia is a rare entity, the overall incidence being 1:15 000 and in Caucasians being 1:23 000. The case is being presented because of its rarity and the simple manner in which it was diagnosed. The investigations conducted were specific and a very economical treatment was rendered considering the low socioeconomic status of the patient.

The case highlights the mental make-up of Asian women for whom fertility is the prime concern, as she opted for management of infertility rather than reconstructive surgery.

CASE PRESENTATION

A 22-year-old woman married for 6 months presented with complaints of amenorrhoea for the past few years. The woman told that she used to enjoy playing with boys and, as she grew up, she was coaxed by her parents to wear feminine clothes. She had started with spontaneous menstruation at the age of 14 years; however, the blood flow was scanty. She had menses for about a year and then amenorrhoea ensued. On questioning, she gave history of some cyclic treatment during adolescence.

On examination on 29 September 2009, her height was 160 cm and weight 45 kg. She had marked hoarseness of voice, temporal balding and facial hirsutism. Local examination revealed hair on chest and male pattern pubic hair. She was found to have a small penis which she told had increased in size in the last few years. Per speculum and per vaginum examination revealed a normal size uterus

and normal length of vagina. She was normotensive and her blood pressure was 110/70 (figure 1).

INVESTIGATIONS

- ▶ Thyroid-stimulating hormone 1.07 miu/ml
- ▶ Luteinizing hormone/follicle stimulating hormone 5.34/3.22 miu/ml.
- ▶ S prolactin 5.04 ng/ml
- ▶ Fasting blood sugar 90 mg%
- ▶ Total testosterone 504.96 (range 14.0–76.0 mg/dl)
- ▶ Dehydroepiandrosterone sulphate 382 µg/dl (range 35–430 µg/dl)
- ▶ 17-A-hydroxy progesterone 120.4 ng/ml (range 0.19–4.69 ng/ml)
- ▶ Ultrasonography—uterus was normal-sized; both ovaries were normal-sized and no adrenal mass was noted.
- ▶ Serum electrolytes were in the normal range.

On analysis, total testosterone was markedly raised but there was no androgen-secreting adrenal or ovarian tumour. Dehydroepiandrosterone sulphate levels were on the higher side of normal and 17-A-hydroxy progesterone was also markedly raised. A diagnosis of 21-hydroxylase-deficient classic congenital adrenal hyperplasia was considered.

TREATMENT

She was started on 7.5 mg prednisolone at bedtime and withdrawal given with 10 mg, twice a day, medroxy progesterone. For three cycles, she was given high-dose oral contraceptive pill containing cyproterone acetate and spironolactone 100 mg, twice a day, to reduce testosterone levels. After 3 months, her S testosterone came down to 166.55 ng/dl. She was continued on prednisolone 5 mg alone. She was given supplemental calcium throughout the therapy.

However, she went to her parent's home and left treatment in-between. She again presented to us on 8 December 2010 with four months amenorrhoea and also complained of manliness. Prednisolone 7.5 mg at bedtime was restarted and progesterone withdrawal was given. After 6 weeks of prednisolone therapy, her S testosterone level dropped to 31.92 ng/dl.

INDUCTION OF OVULATION

She desired conception so induction of ovulation was planned.

From day 2 of spontaneous menstruation, clomiphene citrate 100 mg was started for 5 days along with prednisolone 5 mg. Her follicle size was 22×18 mm on day 13. She ovulated after human chorionic gonadotrophin 5000 IU but did not conceive. In the next cycle, she was started on clomiphene citrate 50 mg from day 2 of the periods. On day 13, her follicle size was 17.8×18 mm.

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Figure 1 Conception in a woman with ambiguous genitalia.

She ovulated and was given supplemental progesterone in luteal phase. She reported on 19 March with 5 weeks amenorrhoea, and her pregnancy test was found to be *positive*. A six weeks viable pregnancy was visualised. An anomaly scan at 16–18 weeks revealed a healthy fetus with no anomalies (figure 2).

OUTCOME AND FOLLOW-UP

The woman stopped her antenatal visits and went to her native village. She came back after 4 months with a history of spontaneous abortion around 21 weeks. An ultrasound scan

immediately prior to abortion showed a healthy fetus with a subchorionic haematoma (figure 3).

DISCUSSION

The incidence of classical congenital adrenal hyperplasia is 1:23 000 live-births in Caucasian women.¹

In women, classical congenital adrenal hyperplasia is characterised by genital ambiguity. It can be due to deficiency of 21-hydroxylase, 11- β -hydroxylase or 3- β -hydroxylase.

Figure 2 Anomaly scan at 16 weeks pregnancy.

Unfortunately, the patient aborted at 21 weeks. Had the girl reached term, we would have learnt about the incidence of gestational diabetes, a higher incidence being reported,⁷ in pregnant women with congenital adrenal hyperplasia.

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graph TD
    A["21  
HYDROXYLASE  
DEFICIENT  
CAH"] --- B["SALT WASTING  
CLASSICAL  
CAH"]
    A --- C["SIMPLE  
VIRILIZING  
FORM OF  
CLASSICAL CAH"]
    A --- D["NONCLASSICAL  
FORM OF CAH"]

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graph TD
    A[21 HYDROXYLASE DEFICIENCY] --> B[DEFICIENCY OF CORTISOL AND ALDOSTERONE]
    A --> C[RAISED ACTH LEVEL]
    A --> D[RAISED 17 HYDROXY PROGESTERONE LEVEL]
    A --> E[RAISED ANDROGENS LEVEL]
  
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graph TD; A[CONGENITAL ADRENAL HYPERPLASIA] --> B[21 HYDROXYLASE DEFICIENCY]; A --> C[11β HYDROXYLASE DEFICIENCY]; A --> D[3β HYDROXYSTEROID DEHYDROGENASE DEFICIENCY];
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A flowchart showing the classification of Congenital Adrenal Hyperplasia (CAH). The top box is labeled "CONGENITAL ADRENAL HYPERPLASIA". It branches into three boxes below it: "21 HYDROXYLASE DEFICIENCY", "11β HYDROXYLASE DEFICIENCY", and "3β HYDROXYSTEROID DEHYDROGENASE DEFICIENCY".

Figure 4 Causes of congenital adrenal hyperplasia.

Learning points

- ▶ Classical congenital adrenal hyperplasia should be considered whenever a woman presents with hirsutism and ambiguous genitalia.
- ▶ A very high testosterone level with no androgen-producing ovarian or adrenal tumour warrants investigations for congenital adrenal hyperplasia.
- ▶ The foremost investigation to be performed when suspecting congenital adrenal hyperplasia is 17- α -hydroxy progesterone level.
- ▶ Supplemental calcium is a must when a woman with congenital adrenal hyperplasia is put on prednisolone.

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