St George's University Hospitals NHS
NHS Foundation Trust

An unusual cause of primary amenorrhoea suggested by the urine steroid profile

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The authors have nothing to disclose

Introduction

Primary amenorrhoea is a pathology with many possible aetiologies. The timing and appropriate first-line investigations for delayed menarche in an otherwise well teenager with secondary sexual characteristics are debatable.

Case report

Presentation

A 15-year-old female of African origin was referred to the regional paediatric endocrine clinic due to: *Parental concern with incidental finding of "? large clitoris".*

History

- The patient's mother noticed the patient's clitoris "looked big" incidentally when she was shown a non-specific rash on the legs without clothes on
- Pubertal development
  - Pubic hair since aged 10 years
  - Breast development since aged 13 years
  - Not achieved menarche
- Past medical history: None apart from acne
- Family history of delayed menarche (mother achieved menarche at aged 17 years)

Examination

- Clinically well and "slim-built"
- Facial acne
- Auxology: Height 172 cm (SDS 1.5), weight 60 kg (SDS 0.41)
  BMI 20.1 kg/m^2 (SDS -0.26)
- Puberty: Tanner stage 4 (B4,P4)
- Clitoris normal size and anatomy
- Rest of general examination unremarkable, in particular, no evidence of hepatosplenomegaly or masses on abdominal palpation

Initial impression

- Signs of hyperandrogenisartion: acne and primary amenorrhoea
- To rule out polycystic ovarian syndrome and late onset congenital adrenal

Initial investigations

Biochemistry

Na, K, Cl, HCO3, U&E, TFT: normal range			
LH	6.2	IU/L	
FSH	8.7	IU/L	
Oestradiol	234	pmol/L	*
Testosterone	5.3	nmol/L	[0.24-2.71]
SGHB	67	nmol/L	[20-110]
T/SHBG ratio	7.9		[0-4]
Prolactin	177	mIU/L	[102-496]
Androstendione	5.4	nmol/L	[2-54]
DHEA-S	1	umol/L	[1.6-7.8]
17-OHP	1.8	nmol/L	*

Pelvic Ultrasound Scan

Small adult uterus with endometrium, left ovary 4.6 ml, right ovary 2.5ml

Urine 24 hour steroid profile (figure 1 and table 1)
showed unexpected findings suggestive of liver abnormality
Report: "High androstenetriol and a-cortolone and low tetrahydrocortisol. Pattern found in association with portal hypertension".

Further Investigations

Repeat urine steroid profiles
Due to the unexpected results from the initial urine steroid profile, the profiles were repeated pre and post dexamethasone suppression (Table 1).

Table 1: Results of initial and repeat urine steroid profile outcomes

Steroid	1st collection	2nd Collection	Post dex	Normal	SD
Androstenedione metabolites	631	329	34	1584	703
Cortisol metabolites	3716	1953	<30	4889	1076
Androstenetriol	2646	1979	316	107	62
Androstenetriol/cort metabolites x 100	71	101		2	
α-cortolone	1592	875	17	738	183
α-cortolone/cort metabolites x 100	42	45		15	

Liver investigations
Liver profile: ALT 239 U/L (0-40), ALP 500 U/L (30-130), GGT 235 U/L (0-38), Alb 26 g/L (35-50), INR 1.5 (0.8-1.1), APTR 1.31 (0.85-1.35)

US liver: Parenchyma heterogeneous, right and left duct dilated, portal vein patent with normal flow. Enlarges spleen 13.8cm

Diagnosis

- Primary amenorrhoea due to previously undiagnosed liver disease

Progress

- Referred to regional liver centre
- Diagnosis of autoimmune liver disease confirmed by antibodies testing and liver biopsy
- Liver function improved since she was started on prednisolone and Azathioprine
- Patient achieved menarche with regular bleeds 6 month's later

Discussion

The initial investigations were guided by the patient's clinical features. The diagnosis was suggested by the urine steroid profile requested to exclude adrenal pathology in the absence of clinical stigmata of chronic liver disease.

The relative increase of a-cortolone in the urine steroid profile has previously been demonstrated in cirrhosis, but raised androstenetriol has not been not previously reported (Figure 2). There was also a low ratio of cortisone (11-oxy) relative to cortisol (11-hydroxy) metabolites, which is not an invariant feature, but is likely to reflect impairment of 11-hyroxysteriod dehydrogenase-1 in hepatocytes.

Although primary amenorrhoea is often physiological in teenage girls, it may also be the first presenting sign of an underlying chronic disease. Careful evaluation is always needed to avoid missing an alternative diagnosis.

Figure 1: Urine steroid profile

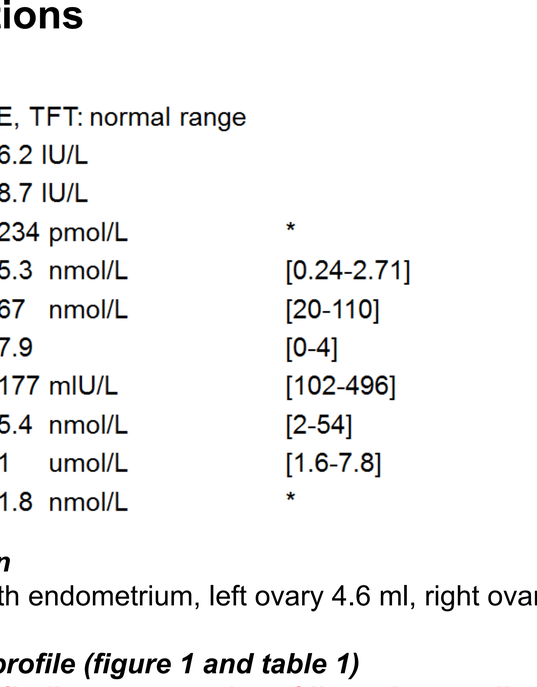
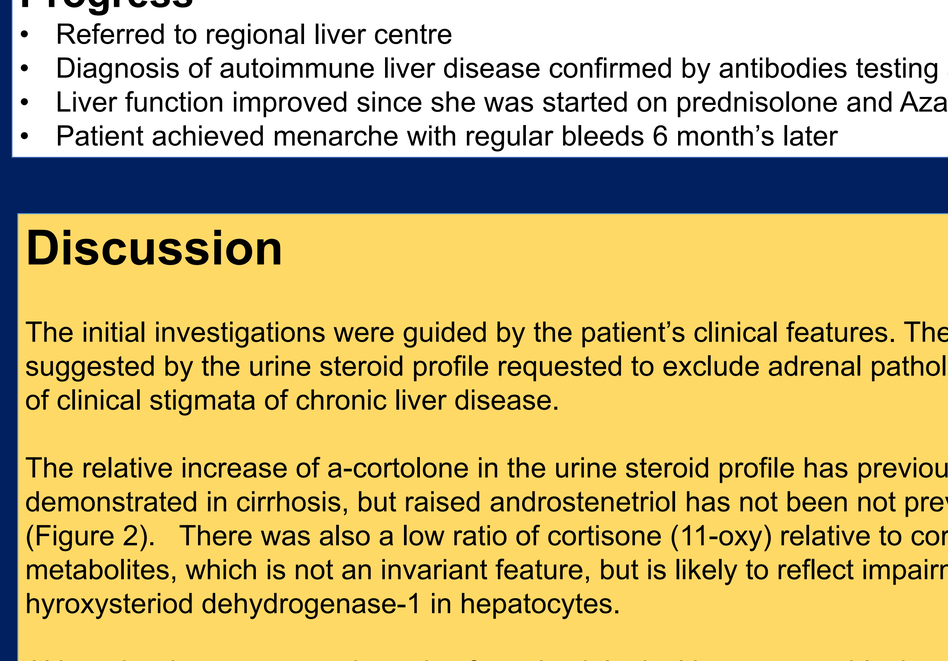


Figure 2: Urinary steroid metabolites



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