This is not surprising since suppression of HPA function in patients using topical steroid preparations is well recorded. James *et al*⁵ found that betamethasone valerate caused lowering of plasma cortisol levels when used with occlusion in inpatients. The same effect has been shown from triamcinolone acetonide without occlusion.⁶ Feiwei *et al*⁷ have shown that plasma cortisol levels in children treated as outpatients with betamethasone valerate tend to be low, although this is not so apparent with adults. Growth retardation, oedema, and Cushingoid features have been noted in babies and children receiving topical corticosteroids.⁸⁻¹⁰

Clobetasol propionate is a highly effective topical corticosteroid preparation.¹¹ A six-month study comparing clobetasol propionate and fluocinolone acetonide in the treatment of psoriasis indicates that it may be even more effective than was shown by earlier short-term trials.¹² It is reasonable to expect that the topical activity of a steroid is correlated with its ability to produce systemic effects, and this has been shown using animal models.¹³

Recent evidence suggests that prolonged application of a topical steroid in adult outpatients may not produce significant adrenal suppression. Wilson *et al*¹⁴ studied plasma cortisol levels in 295 outpatients, 90% of whom were using betamethasone valerate, and concluded that only a few patients so treated would have abnormal HPA function. The use of the insulin stress test in Wilson *et al*'s study and in our outpatient group might have shown abnormal HPA function not shown by simpler methods of assessment. Nevertheless, Munro and Clift¹⁵ used this more rigorous test in studying 40 outpatients comparable with those studied by Wilson *et al*¹⁴ and concluded that there was little effect on adrenal function.

Our results show that when less than 50 g of clobetasol propionate ointment a week is used there may be transient suppression of HPA function, which apparently recovers as the skin heals. This is probably because less ointment is applied and the epidermal barrier is restored, thereby reducing corticosteroid absorption.⁶⁻¹⁶ These observations may explain the results of Walker *et al*,² who found that clobetasol propionate had little effect on plasma cortisol levels. In most of their

patients 5% or less of the body surface area was diseased, and the patients used less than 50 g of ointment a week. It is also conceivable that the timing of their samples—at 14 and 28 days of treatment—allowed any early adrenal suppression to recover despite continuing treatment. This might also account for the apparent lack of systemic activity reported in the other studies cited.

When more than 50 g of clobetasol propionate ointment a week is being used clinicians should be aware of the possibility of adrenal suppression. In children these effects will probably occur with smaller quantities. While short-term adrenal suppression is probably of little clinical significance, long-term suppression should be prevented. Consequently, the most desirable method of using clobetasol propionate in many cases may be to give short intensive courses to induce rapid healing. The systemic and local side effects described by Staughton and August¹⁷ would then be avoided.

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PRELIMINARY COMMUNICATION

The monocystic ovary syndrome

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Summary

Three patients with oligomenorrhoea and hirsutism thought to have the polycystic ovary syndrome were

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found to have only one ovarian cyst. Endocrine findings were similar to those found in the polycystic syndrome, but apart from the single cyst the ovaries were histologically normal; a biopsy specimen of a cyst showed normal follicular appearances and no evidence of luteinisation. These cysts may be the cause of this condition, producing abnormal amounts of ovarian steroids which modify the pituitary response. Further studies are needed, however, to determine this possibility.

Introduction

The syndrome of oligomenorrhoea and hirsutism with polycystic changes in the ovaries has been recognised for many years,^{1 2} although in some cases no obvious ovarian changes are apparent.^{2 3} We report here, for the first time, three cases in which the only ovarian abnormality was a single, and possibly functional, cyst.

Patients and methods

The cases were selected from a study of patients likely to have the polycystic ovary syndrome. Hirsutism was estimated by a method on which 96% of a female outpatient population scored seven or below.⁴ No patient had clinical or biochemical evidence of thyroid, adrenal,

Clinical details and laparoscopic findings in three patients

Case No	Age	Menstrual history				Height (cm)	Weight (kg)	Hirsutism score	Laparoscopic findings		
		Age at menarche (years)	Menstrual frequency (months)	Duration of menses (days)	Previous pregnancy or treatment				Ovarian size (cm)	Side of follicle	Histology
1	25	10	Generally 3 (range 1-6)	2-10	Miscarriage at 14 weeks in 1970	160	112	15	Left 4.8 × 3.2 × 3.2, right 4 × 2.5 × 2.5	Left	Left, part of a normal follicle, 1 corpus atreticum, primordial follicles; right, primordial follicles only
2	29	12	5-7	7	Clomiphene × 2 in 1970, no ovulation; chorionic gonadotrophin × 4 in 1974 caused ovulation	155	52	7	Left 4.5 × 3 × 3, right 2 × 3 × 3	Right	Right, primordial follicles only
3	22	13	1 month until 15 years, then 1-7	5	Volidan for 2 years until May 1974	166	61	18	Left 3.5 × 2.5 × 2.5, right 4.5 × 2 × 2	Left	Left, primordial follicles only

or pituitary disorder. This screening included a test of prolactin secretion. No treatment had been given for six months before investigation and no patient had had a period within two months of an investigation, except as detailed below. Over 48 hours blood samples were taken every 30 minutes for six hours for estimating luteinising hormone, (LH) and follicle stimulating hormone (FSH); every four hours for 48 hours for estimating LH, FSH, testosterone, progesterone, and oestradiol; and every day for estimating sex hormone binding globulin (SHBG).

The LH response to 25- μ g and 100- μ g doses of LH-FSH releasing hormone (LH/FSH-RH) was investigated two or three times either immediately after the 48-hour admission investigations or the day before the laparoscopy, a few months later. LH and FSH,⁵ progesterone,⁶ oestradiol,⁷ testosterone,⁸ and SHBG⁹ were measured as described.

Results

The clinical and laparoscopic features of the three patients are shown in the table. Only one cyst was seen on the surface of either ovary in each case. The cyst was between 5-10 mm in diameter and raised the surface of the ovary. In case 1 it had minor yellowing peripherally. Biopsy specimens were taken at sites away from the cyst. Only primordial follicles were seen in the specimens and the capsular thickness was clearly less than 100 μ m. In case 1 a biopsy specimen inadvertently included part of the cyst wall. This showed normal follicular histological appearances without evidence of luteinisation. In case 1 there was light, abnormal, menstrual bleeding on the second day after operation. Otherwise menses occurred at least five weeks after the operation.

Basal LH values were raised or, sometimes, at the upper limits of normal during all the tests, and the LH responses to LH/FSH-RH were similarly raised when compared to those of control subjects in the early follicular phase of the menstrual cycle. Oestradiol levels were invariably higher than early follicular phase levels and, in general, corresponded to those found near the mid-cycle. Progesterone and FSH values were in the same range as those in the early follicular phase, and testosterone values were normal, but SHBG values were just below normal in cases 2 and 3 and very low in case 1.

Conclusions

The overall endocrine findings in these cases were similar to those previously reported for the constellation of features that may accompany the polycystic ovary syndrome.^{10 11}

The original observation in this study, however, was that some of these cases were associated not with the polycystic ovary but rather with a single and apparently persistent ovarian cyst. Although we cannot guarantee that these cysts were functional it is, nevertheless, attractive to speculate on their potential role in the pathogenesis of the condition. Possibly they may develop during a follicular phase but fail to mature beyond the 5-10 mm stage. They may produce abnormal amounts of ovarian steroids in addition to the oestradiol and these may modify LH and FSH release from the pituitary. We are undertaking further studies to show whether this or a more general defect of the hypothalamic-pituitary-gonadal system is implicated.

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