

A CASE OF HIRSUTISM ASSOCIATED WITH METROPATHIA HAEMORRHAGICA AND MICROCYTIC OVARIES

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Virilisation of ovarian origin need not necessarily be of neoplastic etiology. In the case reported here, there is a rare combination of clinical signs indicating increased oestrogenic activity along with masculinising symptoms.

Case Report. Mrs. K., age 25 years, female, was admitted into the gynaecologic wards of the Stanley Hospital on 26-8-1950 with the following complaints:

- i) Profuse and frequent periods of ten years' duration.
- ii) Growth of hair over the chin and the upper lip for the past seven years.

Previous History. Menstrual—She attained puberty at the thirteenth year. Periods were regular of 28 days' pattern lasting for 4 to 6 days and were not painful. Two years later the menstrual flow became profuse and frequent, at intervals of three weeks, lasting for about a week, with passage of clots per vaginam. In

1943, when she was 18 years old, the periods became more profuse and prolonged lasting for 15—20 days with a 30 day cycle. Progesterone therapy, 10 mg. intramuscularly on alternate days for a week, was followed by three months' amenorrhoea. Later on, menorrhagia continued as before and in 1945, dilatation and curettage was performed in Bombay. A diagnosis of metropathia was made on histologic examination of the endometrial scrapings. Two months later, the complaint recurred. Hormonal treatment, first with progesterone and later in 1949 with chorionic gonadotrophin, proved to be ineffective. Supportive antianaemic treatment was given during most of this period. She was married at the age of 18 and since the same year she has noticed gradual increase of hair from downy growth to marked trichosis over the chin, upper lip and round the areola of the breasts. There is no loss of libido. She has had no children or abortions.

General Examination. Slightly obese, average statured individual, with hypertrichosis on the upper lip and chin, fairly longish hair in the midsternal region and round the nipples; male type of escutcheon and moderate growth of hair on the arms and legs. There was no appreciable change in the voice. No atrophy of the breasts. On abdominal examination, no striae. No palpable masses were felt.

Vaginal Examination. No hypertrophy of the clitoris; cervix was normal, uterus anteverted and ante-flexed, normal in size; both ovaries palpable—right one bigger than the left and not tender.

Investigations. Haemoglobin: 55%. Blood Pressure: 110/74 mm. of mercury. Urine: No albumin, no sugar. Hormonal estimation of pregnanediol and 17-ketosteroids in the urine were within normal limits. X-ray skull: Normal hypophyseal fossa. Intravenous pyelography: Nil abnormal. No distortion of upper calyces of renal pelvis.

A provisional diagnosis of Thecoma was made and a laparotomy was decided on 28-8-50.

Operation Notes. Under heavy spinal, 1.4 ml. of 1 in 200 Nupercaine, right paramedian incision was made. On opening the abdomen, the uterus was found normal in size and position. On the fundus of the uterus, near the right cornu, a small firm nodular swelling was noticed. It could not be enucleated, but was excised (? adenomyosis). The right ovary was enlarged (3" X 2" X 1"), heavier than normal, distorted in

shape, of rubbery consistency and granular surface. The left ovary was bigger than normal and its lateral half was hard and gritty. No fluid could be aspirated from the right ovary. Right oophorectomy with resection of the outer half of left ovary was done. No evidence of endometriosis was found anywhere else in the pelvis. Appendix was thin and long and was removed. On palpation in the region of the kidneys no abnormality could be made out. Abdomen was closed in layers.

Naked eye appearance of the right ovary (Fig. 1). On section, greyish in color; shows multiple small cysts arranged along the outer portion of the cortex. None of the follicles was larger than a centimeter in diameter.

Micr.: (i) Excised nodule from the fundus of the uterus shows endometrial glands in the proliferative phase surrounded by stromal cells and myometrium, adenomyosis (Figs. 2 & 3).

(ii) Ovary: Numerous atretic follicles lined by a few layers of granulosa cells with peri-follicular proliferation of theca cells (Figs. 4 & 5).

The post operative period was smooth and the patient was discharged on 15th day after the operation.

Follow up. Seen on 11-5-1951. First period about a month after the operation was profuse with clots and lasted for 6 days. Subsequently, the periods were quite normal, 4-6/30 days, moderate flow, occurring at regular intervals. There was no appreciable improvement in the hirsutism.

When seen again in October 1952 menstrual history was normal. Hir-

suitism not regressed.

Discussion. This case is peculiar in as much as there is masculinisation associated with evidence of hyperoestrinism, as shown by cystic glandular hyperplasia of the endometrium and adenomyosis of the uterus. Virilisation in women may be brought about by (i) Cushing's syndrome or Basophil adenoma of the pituitary, (ii) hyperplasia or neoplasm of the adrenal cortex; and (iii) arrhenoblastoma and adrenal rest tumor (or virilising lipoid cell tumor of Barzilag) of the ovaries. In the last group of cases, obviously, the ovaries will show evidence of neoplastic change on histologic examination. Geist & Gaines reported ovarian enlargement due to diffuse luteinisation (not tumor formation but luteinised follicles) associated with masculinisation. Virilising symptoms in such cases were attributed to hyperthecal activity in the ovaries. Subsequently, similar case reports were published by Culiner & Shippel, Shippel and Beattie, et al. In these cases 17-ketosteroids content of urine was normal. It has been pointed out by Iverson that there is striking similarity—morphologically, embryologically, functionally and chemically—between the theca-lutein cells of the corpus luteum, interstitial cells of arrhenoblastoma and cells of adrenal tumor of the ovary. He concludes that "androgens are produced in the ovary and more specifically by the theca-lutein cells". This is not surprising when we consider the fact that the "pure" theca cell tumors do not produce oestrogens (Traut and

Marchetti). Besides, the theca cell tumors may exhibit at one and the same time symptoms of both marked masculinisation and feminisation—with decidual reaction in the endometrium as reported by Trowmbly. Shippel suggests that this may be due to a single androgenic hormone from these theca cells which simulates actions of all the three sex hormones—oestrogen, testosterone and progesterone.

Virilism and Swiss-cheese hyperplasia of the endometrium is described by Rheuby in a patient 21 years old with virilism, menorrhagia, hoarseness of voice, hypertrichosis and hypertrophied clitoris. Curettage revealed thick endometrial scrapings suggestive of malignancy. On laparotomy, the uterus was normal and the ovaries were enlarged. Total hysterectomy with bilateral salpingo-oophorectomy was done. The endometrium showed severe oestrin type of hyperplasia. The ovaries on section showed numerous follicles in various phases of development; marked theca-lutein reaction was seen on histologic examination. No diminution of hypertrichosis or macroclitoris occurred in this case following the operation. Shippel mentions a patient, 19 years of age, complaining of severe menorrhagia and hirsutism, normal breast development and clitoris in whom the endometrial scrapings proved to be oestrogenic. In such cases, according to him, there is disturbance of normal balance between the thecal and granulosa cell activity. When granulosa cell activity increases there is cystoglandular hyperplasia; and when the oestrogen level drops or

androgen level rises—cystoglandular hyperplasia with signs of virilism appear due to the excessive thecal activity.

Maculinisation with bilateral enlarged ovaries is now considered as a syndrome since the ovaries in most of these cases show thecal hyperplasia, hypertrophy and luteinisation. The hyperthecal activity in such cases is believed to be due to stimulation by the gonadotrophic hormone of the pituitary (Geist & Gaines; Culiner & Shippel). Though these writers believe that altered menstrual function and masculinisation may be brought about by the thecal hyperplasia, the treatment of this condition remains unsatisfactory. In most of the cases, partial or complete resection of the ovaries was done with correction or relief of menstrual dysfunction but with no regression of the virilising symptoms.

Summary

A case of hirsutism associated with metropathia haemorrhagica and microcystic ovaries is described and briefly discussed.

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Fig. 1.: Section of the right ovary showing multiple small cysts along the outer portion of the cortex.

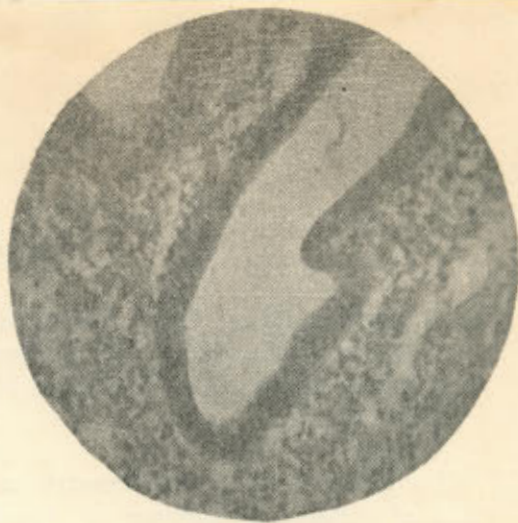


Fig. 3.: Figure 2 magnified showing endometrial glands in the proliferative phase surrounded by stromal cells (X 130).



Fig. 2.: Adenomyosis—showing endometrial glands with the surrounding stroma and muscle (X 40).

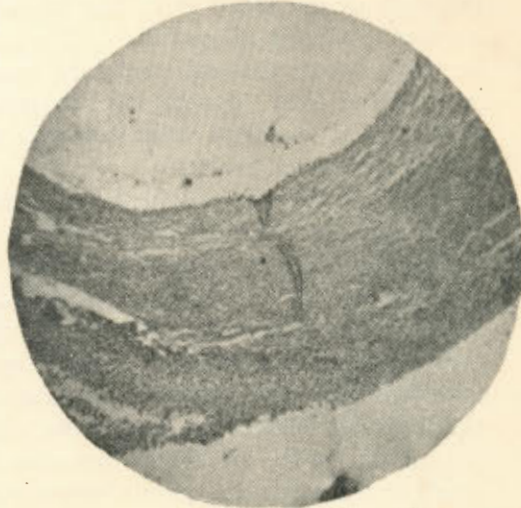


Fig. 4.: Photomicrograph of the cystic follicle (X 40).

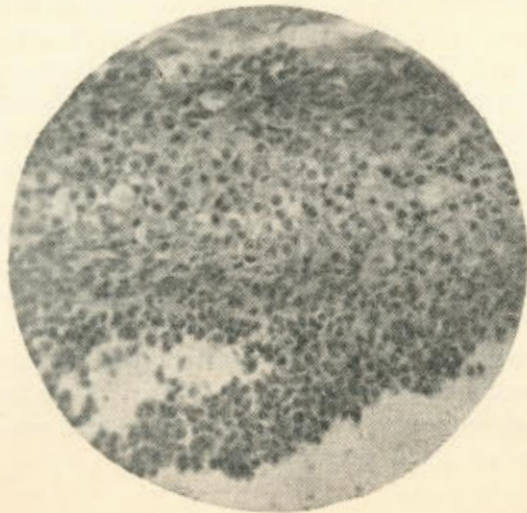


Fig. 5.: Figure 4—magnified—showing the cystwall lined by few layers of granulosa cells and perfollicular