Precocious Puberty due to Granulosa Cell Tumour of Ovary

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PRECOCIOUS puberty is an arresting and dramatic phenomenon which has always stimulated the interest of the clinician. References in the literature as far back as the 17th century are not uncommon.

Textbooks have, until recently, given the subject scant consideration, although in 1910 Blair-Bell[1] wrote as follows: "In precocious puberty children have been known to menstruate from birth onwards and to be fully developed when a few years of age, so far as the objective signs of sexual maturity are concerned. Such children have been found to possess ovarian tumours which have undoubtedly given rise to abnormal and precocious ovarian stimulation."

Comparatively recent work on the physiology of the ovary and the isolation of its two hormones has given an added interest to the subject and the cases recorded are rapidly growing in number. It is becoming increasingly evident that a majority of these cases are associated with tumours of the ovary, and of these growths the so-called granulosa cell tumour is the commonest (Novak and Gray[2]). In this connexion a recent article by Meigs and Parsons[3] may be briefly summarized thus: A granulosa cell tumour is one composed of cells resembling very closely the cells of the granulosa of the normal Graafian follicle. They may be of almost any size, but are usually about that of an orange, and are nearly always unilateral. The tumours are usually solid with cystic areas in them. All types of granulosa cell tumours secrete oestrin, but the relative amount, and whether the secretion is continuous or not, is unknown. From the point of view of diagnosis the presence of oestrin in the

urine of precocious puberty or of women past the menopause should be confirmatory.

Granulosa cell tumours may manifest themselves at any time of life; they may cause precocious menstruation during childhood, abnormality of the menstrual cycle during the reproductive period, or uterine bleeding long after the menopause, but the induction of an abnormally precocious puberty is clinically their *pièce de résistance,* and for that reason we consider this case worth reporting.

J. M., a female child of 17 months, was seen at the outpatient department of the Royal Devon and Exeter Hospital on August 16th, 1933. The mother stated that the child had had a rapidly increasing distension of the abdomen for the previous 10 days. There was not any vomiting and the child was said to be quite well otherwise. She had been taking her food well and the bowels were open three or four times a day. Uterine bleeding had been absent up to this time.

The patient was admitted to hospital and found to have an enormous distension of the abdomen. There was a small umbilical hernia and veins were unusually prominent on the abdominal wall. The percussion note was dull with the exception of the epigastrium when the patient was lying on her back and there was a well-marked fluid thrill.

It will be seen from the photograph (No. 1) taken in September 1933 that the general nourishment of the child was good. Her facial expression was that of an older girl and the secondary sexual characteristics were those of puberty. Thus the breasts were beginning to develop, the labia were larger than normal with dark hair present on them, and the clitoris was well developed. Her weight in a nightdress was 1 stone 11 pounds.

During the 5 weeks she was in the hospital before being operated upon her temperature was slightly irregular, rising to 100°F. on three occasions; the pulse-rate was rapid, being consistently in the region of 130 to 140 beats per minute.

On the 10th day after admission it was noticed that the child had a blood-stained vaginal discharge. Microscopically this was seen to contain mucus in moderate amount, epithelial and polymorphonuclear cells in addition to large numbers of red cells.

Radiograms were taken of the skull and chest. The pituitary fossa was not enlarged nor could any abnormality of the thymus be detected.

A diagnosis of a tumour of the ovary was made and an operation was performed on October 2nd, 1933.

Operation.

After 5 pints of clear serous fluid had been removed from the abdominal cavity a solid tumour of the right ovary was found. It was about the size of an orange with a smooth surface, white in colour and unattached to surrounding structures.

The uterus and left ovary were normal in size and appearance. There was not any evidence of secondary deposits anywhere and enlargement of the adrenals could not be detected.

The tumour and Fallopian tube were removed, and the child was discharged from hospital 15 days later.

Convalescence was uneventful with one notable exception. On the 3rd day after operation bleeding started again and lasted 7 days. The flow had the same characteristics as before and started 27 days after the first period.

After History.

The child attended the out-patient department after discharge and was last seen on August 30th, 1934. The mother reported that there had not been any further menstrual loss and that the child was quite well although she had been a little irritable at times. The abdomen was normal in size; the umbilicus was still slightly prominent but a hernia could not be detected.

With the exception of a fine down on the labia, pubic hair was absent, and the breasts were not now enlarged. These points are well shown in photographs Nos. 2 and 3 which were taken on September 4th, 1934. Her weight in clothes was 1 stone 12 pounds.

Tumour.

The external appearance was that of a smooth white growth, oval in shape and measuring 2 inches by 2 inches by 3 inches. On section it was found to be solid and of a homogeneous consistence, rather soft to the touch and pinkish in colour. Sections were made by Professor G. R. Cameron of University College Hospital, London, and he reports as follows:

Microscopical appearance. The ovarian tissue is almost completely replaced by tumour cells, a few tiny follicles persisting at the periphery

of the ovary quite distinct from the tumour. The new growth, at first sight, appears to have no pattern but closer examination discloses a series of large and small rounded masses of cells resembling huge follicles. In one section it was possible to trace the outgrowth of such cells from the periphery of a small but definite follicle. The cells so grouped are mostly cuboidal but soon assume elongated and in places spindle forms. In a few cases the follicular cells are arranged concentrically at the periphery of the follicle but all such arrangement is lost towards the centre. Few blood-vessels are present and there is no evidence of new fibrous tissue (Van Giesen stain). Sections stained with Sudan III fail to show lipoid filled spaces in the tumour and no tumour cells contain fat particles.

In view of the history 2 feminising ovarian tumours have to be considered: (1) Granulosa cell tumour and (2) Theca tumour—Fibroma thecocellulare xanthomatoides.

In the absence of any tendency to fibrosis and of lipoid deposition in the tumour the theca tumour seems to be excluded. Although the histological features are not absolutely typical of the granulosa cell tumour it must be remembered that atypical or diffuse varieties of the latter have been described and I believe this case to be such.

In reviewing this case it is of some interest to speculate as to what factor determined the onset of menstruation. The tumour from its size must have been present for some months, but there was apparently an increase in its activity a short while before the case came to our notice as is suggested by the rapid appearance of the ascites.

The post-operative uterine bleeding which occurred on the 3rd day after the operation is of interest, for although almost exactly 4 weeks had elapsed since the first period, it is possible that the second was an oestrin deprivation phenomenon.

Summary

1. A case of precocious puberty is recorded occurring in a girl aged 17 months.

2. Uterine bleeding together with secondary sex characteristics were present.

3. A tumour of the ovary of the granulosa cell type was removed by operation.

4. The child made an uneventful recovery and reverted to normal for her age and sex.

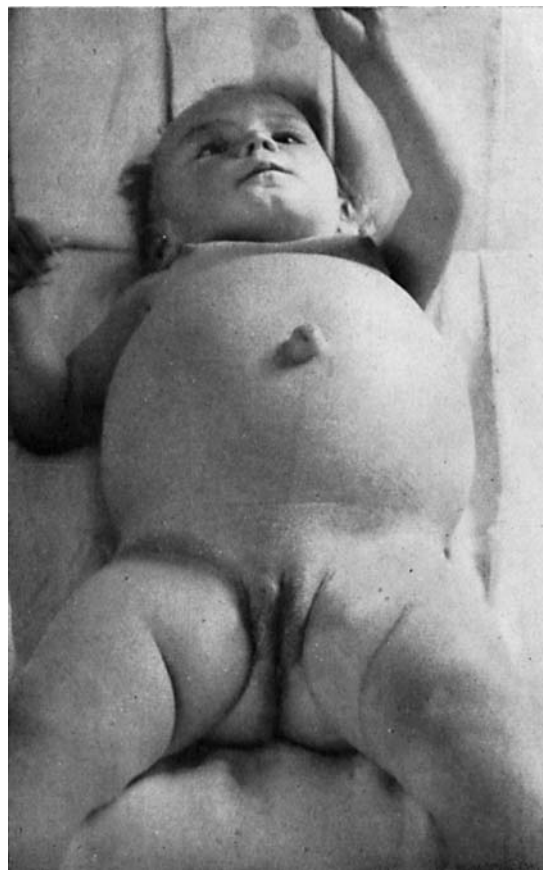

FIG. 1

Patient before operation

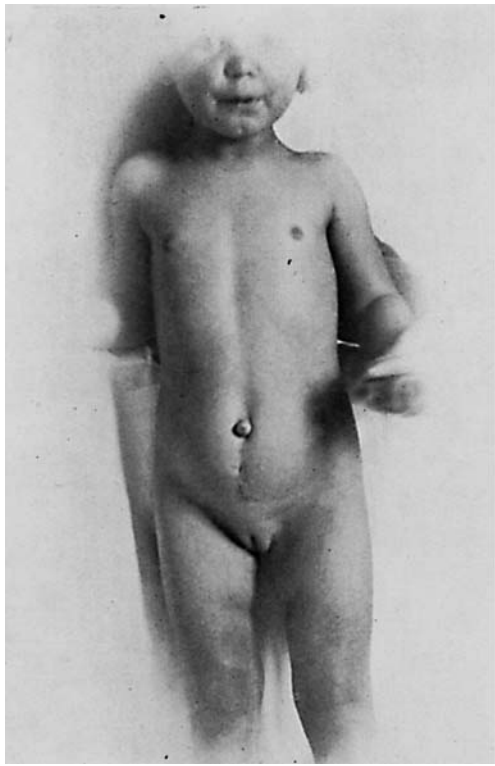

FIG. 2

FIG. 3

Patient a year after operation

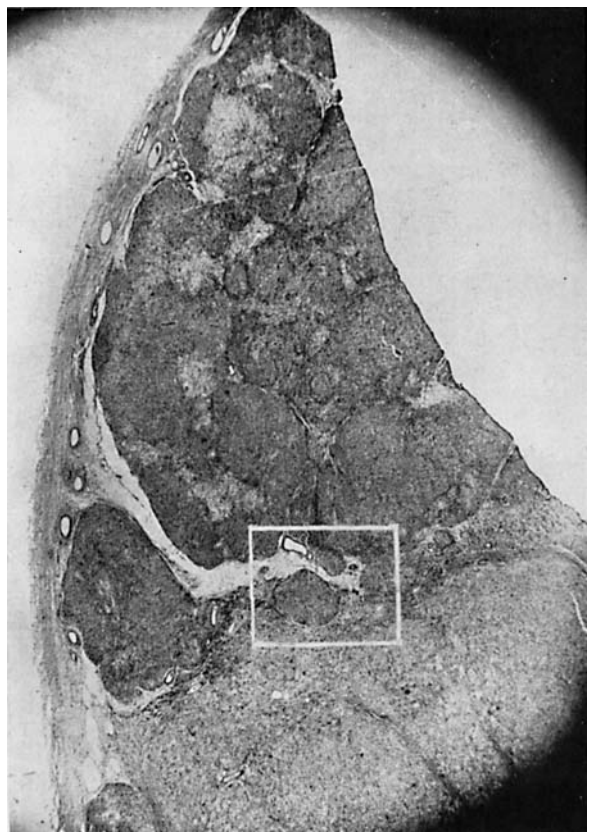

FIG. 4

Low power magnification of tumour showing folliculoid structure. × 10.

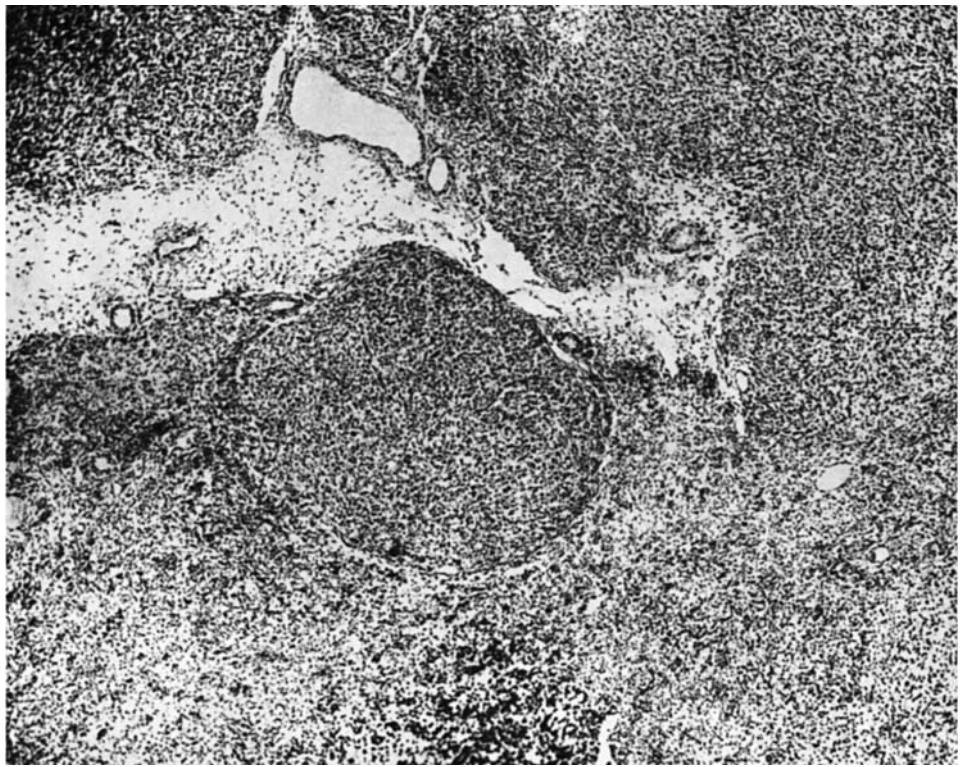

FIG. 5

Folliculoid mass surrounded by more diffuse tumour. × 58.

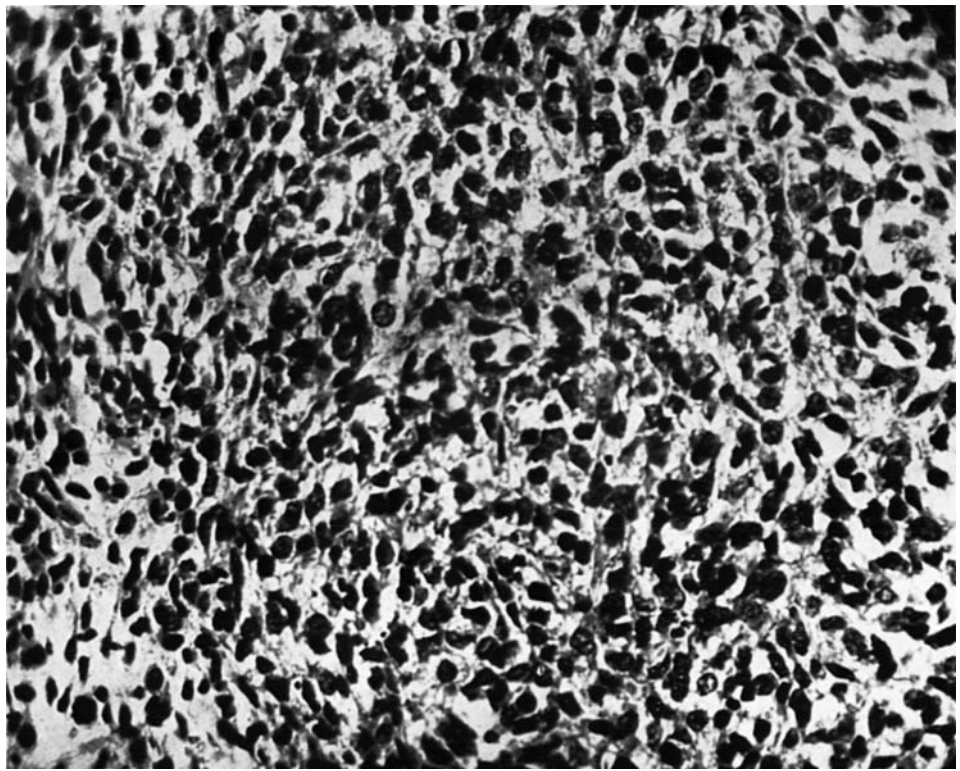

FIG. 6

High power detail of cells in folliculoid mass of *Fig.* 5. × 444.

In conclusion we wish to thank Professor Cameron for the trouble he has taken in examining and reporting on the microscopical appearances of the tumour.

References

1. Blair-Bell, W. "The Principles of Gynaecology," 1910.
2. Novak, E., and L. A. Gray. *Amer. Journ. Obstet. and Gynecol.*, 1936, xxxi, 212.
3. Meigs, J. V., and L. Parsons. *New Eng. Journ. of Med.*, April 1937.