Histopathological Findings of the Ovaries in Anovulatory Women

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HIRANO, M., SUZUKI, K., HIGASHIHWAI, H. and SUZUKI, M. Histopathological Findings of the Ovaries in Anovulatory Women. Tohoku J. exp. Med., 1976, 120 (4), 339-344. — Wedge resection of the ovary was carried out in 45 anovulatory women to study the correlation between the degree of disturbance of ovulation and the histopathological findings. Polycystic ovary was always found in patients with anovulatory cycles. The ovaries in grade 1 amenorrhea showing withdrawal bleeding in response to gestagen alone belonged to the nonspecific type, polycystic type and sclerotic type. These histological changes were relatively mild in many cases. The ovaries in grade 2 amenorrhea showing withdrawal bleeding in response to estrogen and gestagen but not to gestagen alone belonged to the non-specific type, polycystic type, sclerotic type, atrophic type and streak type. Even within the same histological entity, the histological findings of the ovaries were more pronounced in grade 2 amenorrhea than in grade 1 amenorrhea. The patients with primary amenorrhea had only hypoplastic and aplastic ovaries with marked histological abnormalities. —— ovary; anovulatory woman

Though endocrinological studies on the hypothalamus-pituitary-ovarian axis have resulted in remarkable progress in recent years, scarcely any studies have been carried out on the ovaries of anovulatory women. In order to conduct a more effective induction of ovulation in anovulatory women, it is necessary to clarify the histopathological findings of the ovaries in these women. In 45 anovulatory women in whom various attempts hardly succeeded in inducing ovulation, wedge resection of the ovary was carried out and the ovarian tissue was histopathologically compared with ovarian tissue from 16 women who had a history of delivery and regular menstrual cycles and were entirely free from disturbances of ovulation. The tissue was obtained at laparotomy for other disease which occurred during the age in which there was a possibility of pregnancy. The correlation between the degree of disturbance of ovulation and these histological findings was studied and several pertinent results were obtained.

Materials and Methods

Materials. Control ovarian tissues were taken from 16 women between the ages of 20 and 30 with a history of delivery and regular menstruation. They were presumably free...
from ovulatory disturbances at laparotomy for gynecological diseases other than those of the ovary such as uterine myoma and cervical carcinoma. In 45 women between the ages of 20 and 34 with the diagnosis of anovulation based on menstrual history and basal body temperature curves in whom attempts at induction of ovulation by various drugs had been almost unsuccessful, ovarian tissue was obtained by wedge resection. In 10 of these cases, anovulatory cycles were seen with menstruation without BBT patterns indicating ovulation. Grade 1 amenorrhea with withdrawal bleeding in response to gestagen administration was seen in 8, grade 2 amenorrhea with withdrawal bleeding in response to estrogen and gestagen administration but not gestagen alone was found in 19, and primary amenorrhea without natural menarche until after 18 years of age was found in 8.

**Method.** After fixation with 10% formalin, the ovarian tissue was embedded in paraffin and sections of 4 μm in thickness were prepared along the long axis from the free edge to the hilus of the ovaries. Hematoxylin-eosin stain, Azan-Mallory stain, and Elastica-Masson (Goldner's modification), Alcian blue and PAS double stain were carried out. Special attentions were paid to those histological findings of the ovaries which might be closely related with anovulation such as thickening of the tunica albuginea, sclerotic changes and thinning of the cortex, frequency of appearance of various follicles, thickening of the granular membrane and theca interna, degree of luteinization of the granular membrane, theca interna, theca externa and cortex, and presence or absence of corpus luteum and corpus albicans.

**RESULTS**

**Histopathological classification of the anovulatory ovary**

As a result of histological comparison between the ovaries from anovulatory women and control subjects, those of anovulatory women were classified into the following 7 types:

1. **Non-specific type ovary:** An ovary without specific findings to distinguish it from a normal ovary except for the absence of the corpus luteum.

2. **Polycystic type ovary:** Numerous cysts are found macroscopically and primordial follicles, growing follicles and atretic follicles are found more frequently than in the normal ovary with predominance of luteinization in atretic follicles and the cortex (Fig. 1).

3. **Sclerotic type ovary:** The numbers of primordial follicles, growing follicles and atretic follicles are somewhat smaller than those in the normal ovary. There was marked proliferation of the cortical connective tissue (Fig. 2).

![Fig. 1. Polycystic type ovary (low magnification).](image-url)
4. Atrophic type ovary: The number of growing follicles and atretic follicles is extremely small. Thinning and sclerotic changes of the cortex are noted. The tunica albuginea is markedly thickened and luteinization is not found (Fig. 3).

5. Hypoplastic type ovary: Primordial follicles are quite numerous and growing
correlation between the degree of disturbance of ovulation and histological entities of the ovary

The patients with anovulation are classified into 4 groups according to the degree of disturbance of ovulation in order to correlate the clinical classification with histopathological findings; anovulatory cycle, grade 1 amenorrhea, grade 2 amenorrhea and primary amenorrhea (Table 1). All of the 10 patients with anovulatory cycles had polycystic ovaries. Among 8 patients with grade 1 amenorrhea, the non-specific type was found in 2 cases (25%), the polycystic type in 4 cases (50%) and the sclerotic type in 2 cases (25%). Polycystic ovaries in many of the cases of grade 1 amenorrhea resembled the non-specific type ovary. In cases of grade 2 amenorrhea, every type of the ovary was seen except for the hypoplastic...
TABLE 1. Correlation between the degree of disturbance of ovulation and histological classification of the ovaries in anovulatory women

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<thead>
<tr>
<th>Classification of ovaries</th>
<th>Degree of disturbed ovulation</th>
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<tr>
<td></td>
<td>Anovulatory cycle</td>
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<tr>
<td>Non-specific type</td>
<td>2</td>
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<tr>
<td>Polycystic type</td>
<td>10</td>
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<tr>
<td>Sclerotic type</td>
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<td>Atrophic type</td>
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<td>Hypoplastic type</td>
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<td>Streak type</td>
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<td>Agenetic type</td>
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and agenetic types. Among 19 cases, the non-specific type was seen in 5 cases (26%), the polycystic type in 5 cases (26%), the sclerotic type in 4 cases (21%), the atrophic type in 2 cases (11%), and streak type in 3 cases (16%). Sclerotic changes were more pronounced in the polycystic type in grade 2 amenorrhea than in grade 1 amenorrhea. Among 8 cases of primary amenorrhea, the hypoplastic type was seen in 3 cases (38%), and the agenetic type in 5 cases (25%).

The degree of clinical disturbance of ovulation was studied in each of the 7 types of anovulatory ovaries in our classification (Table 1). The non-specific type ovary was seen only in 7 cases; in 2 cases (29%) of the cases of grade 1 amenorrhea and 5 cases (71%) of the cases of grade 2 amenorrhea and it was not seen in anovulatory ovulation or primary amenorrhea. Among 19 cases of polycystic ovaries, the anovulatory cycle was seen most frequently in 10 cases (53%) or in all cases of anovulatory cycle, followed by grade 1 amenorrhea in 4 cases (21%), grade 2 amenorrhea in 5 cases (26%), and in no cases of primary amenorrhea. Six cases with sclerotic ovary were composed of 2 cases (33%) of grade 1 amenorrhea and 4 cases (67%) of grade 2 amenorrhea. The atrophic type ovary was seen only in grade 2 amenorrhea. The hypoplastic type and agenetic type ovary were seen in primary amenorrhea alone.

DISCUSSION

Though histological studies have been conducted on the ovaries of patients with special syndromes such as gonadal dysgenesis (Jones 1962; Greenblatt et al. 1967) polycystic ovary (Goldziewer and Green 1962; Dokumov and Dashev 1963), primary amenorrhea (Zourlas and Comninos 1971; Black and Govan 1972) and gonadotropin-resistant ovary (Campenbou et al. 1972), scarcely any detailed histopathological studies have yet been conducted on the ovaries of anovulatory women of a variety of causes with reference to the degree of clinical disturbance of ovulation. Except for the report of Tanaka (1972) on the ovaries of 15 anovulatory women, all studies on the ovaries of anovulatory women have dealt with endoscopic and macroscopic findings supplemented with some histopathological
features (Nishimura et al. 1970).

At first, we have therefore histopathologically compared the ovaries in anovulatory women and control women with the possibilities of pregnancy, and classified the ovaries of anovulatory women into 7 types, according to the grade of the deviation from normal histological findings of the ovary. We then studied the relationship between such morphological classification and degree of disturbance of ovulation. The absence of non-specific ovaries in patients with anovulatory cycles with clinically mild disturbances of ovulation is probably due to the selection of the cases in which ovulation cannot be induced by drugs and the exclusion of cases of ready induction of ovulation by drugs. The presence of the non-specific ovary in some cases of grade 1 and grade 2 amenorrhea is probably due to the fact that our observation is based on an ovarian tissue specimen obtained by wedge resection precluding an overall view on the ovary or the changes of the ovarian medulla, where abnormalities in the distribution of blood vessels may be present without relation to changes in the ovarian cortex. Further studies are necessary on this point. The atrophic type and streak type ovaries were not found in grade 1 amenorrhea. Within the same entity, the histological findings of ovaries were more pronounced in grade 2 amenorrhea than in grade 1 amenorrhea. In primary amenorrhea with the most serious disturbance of ovulation, however, only hypoplastic and agenetic ovaries were found. Our present histopathological classification of the ovary of anovulatory women thus appears to be approximately parallel to clinical classification of the degree of disturbance of ovulation. Further studies on a larger number of cases would clarify still open questions in the present study.

References