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Endometrial Carcinoma Associated with Stein-Leventhal Syndrome

—Two cases report—

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INTRODUCTION

Stein-Leventhal syndrome is a clinicopathological entity characterized by chronic anovulation and sclerotic ovaries[1,2]. Clinically, the affected patients typically present their third decade with a history of premenarchal obesity and postmenarchal onset of oligomenorrhea or amenorrhea, infertility, and clinical evidence of increased androgen production[1~3]. In some patients, there are estrogenic phenomena such as menometrorrhagia with or without endometrial hyperplasia or carcinoma[2~5]. Several studies have indicated that there may be an increased incidence of ovarian neoplasia in polycystic ovaries[6,7].

Recently, we experienced two cases of polycystic ovaries assotiated with endometrial carcinoma in premenopausal women, who had clinical characteristics of Stein-Leventhal syndrome; one of the cases had additional serous cystandenofibroma.

CASES REPORT

Case 1.

Clinical history: The patient was a 30-year-old married woman who had a history of primary infertility during 5 years, secendary amenorrhea, and menstrual irregularity. Physical examination revealed mainly truncal obesity. She revealed secondary female sex characteristics without enlargement of clitoris, hirsutism, or virilism.

Hormonal studies showed Testosterone 0.9 pg/dl (0.2-0.8 pg/dl), LH 11.67 mIU/ml (4-20 mIU/ml), E2 85.5 pg/ml (30-400 pg/ml), and DHEA-sulfate 110.9 μg/dl (82-338 μg/dl).

Under the diagnosis of grade I adenocarcinoma of endometrium in curettage specimen, total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed.

Pathologic findings: The right and left ovaries were symmetrically enlarged and measured 8.0×5.0×3.0 cm and 7.0×4.5×2.5 cm in size, respectively (Fig. 1). They were solid and cystic. The solid portion revealed variable sized, small subcapsular cystic follicles and extensive thickening of the cortex (Fig. 2). The cystic portion was unilocular and contained several papillary projections. Microscopic examination of the ovaries revealed multiple cystic follicles with thick layer of luteinized theca interna cells and stromal hyperplasia. There was no stigmata of ovulation, such as corpora lutea and corpora albicantia. The cystic portion was that of serous cystadenofibroma. The uterus measured 10.0×5.0×3.0 cm in size and weighed 100 gm. On section, the endometrium was diffusely thickened and pinkish friable. It measured 0.5 cm in thickness. Microscopic examination of endometrium revealed variable degrees of endometrial glandular proliferation ranging from adenomatous hyperplasia to adenocarcinoma. Multifocal squamous and morular

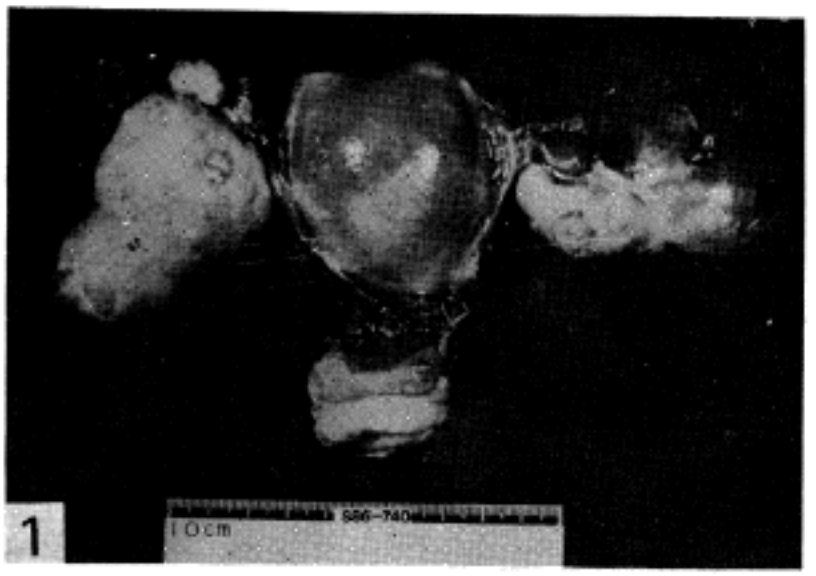

Fig. 1. Polycystic ovaries, fallopian tubes and uterus from case 1; The ovaries are symmetrically enlarged with thick capsule.

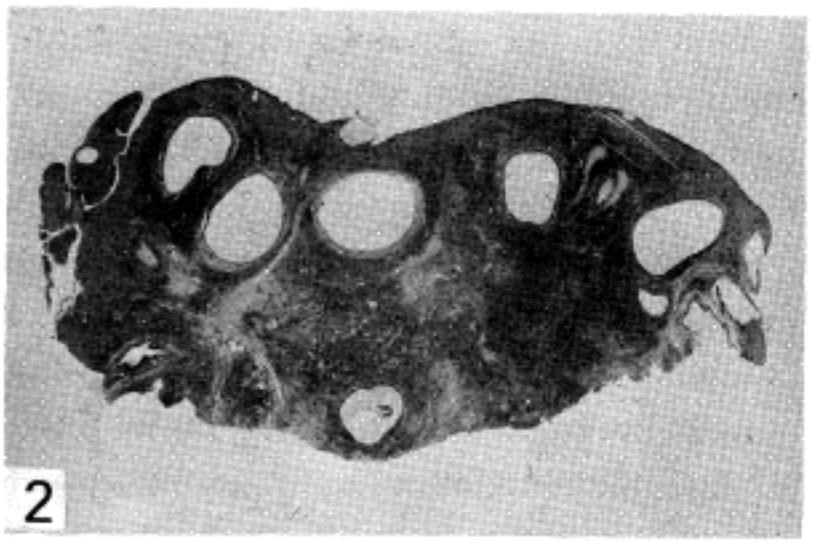

Fig. 2. Several cystic follicles are situated in the subcortical portion of the ovary of case 1.

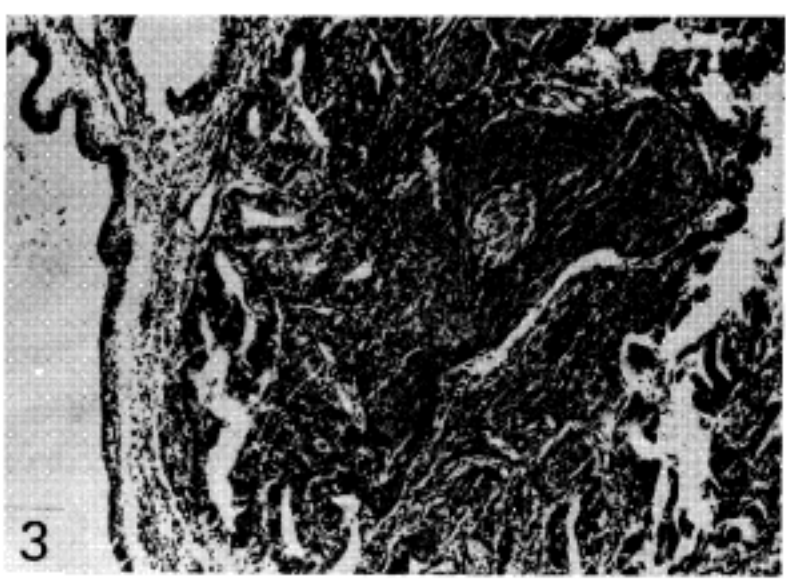

Fig. 3. Well differentiated endometrial adenocarcinoma with squamous or morular metaplasia in case 1 (H&E, ×100).

metaplasia were observed (Fig. 3).

Case 2.

Clinical history: The patient was a 38-year-old woman who visited the hospital because of primary infertility and continuous vaginal spotting for 15 days. She had a history of amenorrhea and irregular menstruation. Physical examination revealed obesity, and other findings were unremarkable. There were no enlargemant of clitoris, hirsutism and virilism.

Hormonal study revealed FSH 7.29 mIU/ml, LH 10.8 mIU/ml, Testosterone 0.69 pg/dl, and E2 38.0 pg/ml. A diagnostic endometrial curettage revealed well differentiated adenocarcinoma. and total abdominal hysterectomy and bilateral salpingo-oophorectomy were done.

Pathologic findings: The right and left ovaries measured 5.0×2.0×1.5 cm and 4.5×2.5×1.5 cm, respectively. They were white and the capsule was tough. There were several translucent subcortical cystic protrusion. Cut section reveased many small sized systic follicles in the subcortical region (Fig. 4). The medullary portion was yellowish and solid. No corpora lutea were found. Oviducts were unremarkable. The follicles were lined by granulosa cells and luteinized theca interna cells (Fig. 5). There was no corpora lutea or corpora albicantia. The stromal hyperplasia was marked, but there was no evidence of stromal luteinization The endometrial cavity revealed diffuse thickening of endometrium with polypoid appearance. Microscopically, the ovaries showed diffuse thickening of tunica albuginia and numerous subcapsular cystic follicles. The endometrium revealed adenomatous hyperplasia and frank adenocarcinoma which have cribriform pattern (Fig. 6). No myometrial invasion was noted.

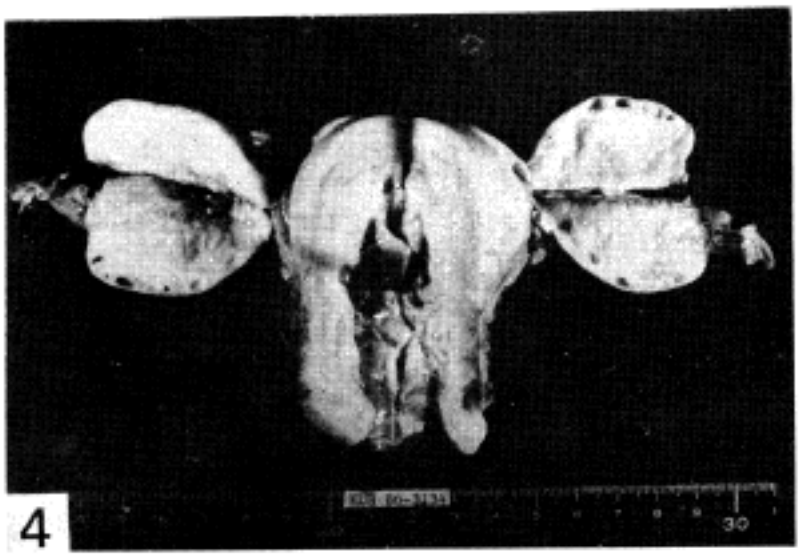

Fig. 4. Uterus and both adnexae of case 2; The ovarian surface shows several subcortical cystic follicles and the endometrial cavity shows diffuse thickening with polypoid appearance at the fundic portion.

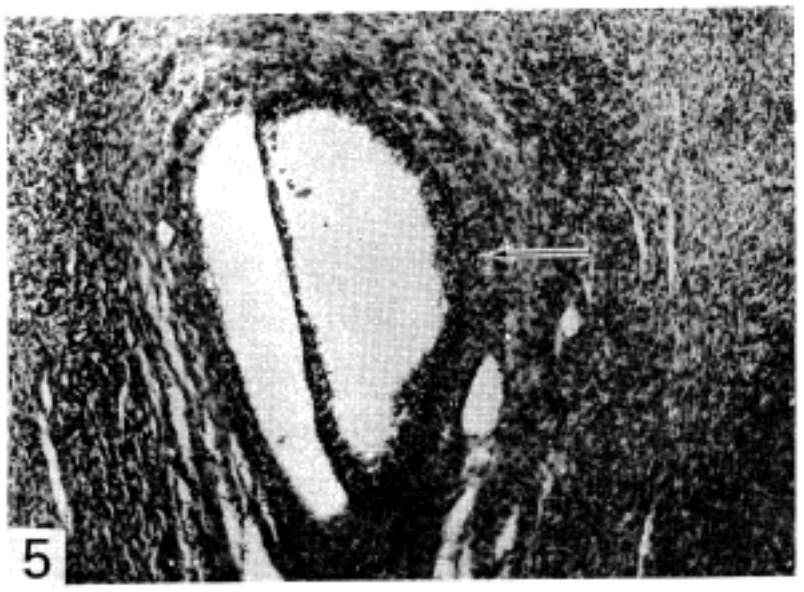

Fig. 5. The arrow indicates hyperplastic theca interna cells around the cystic follicles (case 2) (H&E, ×250).

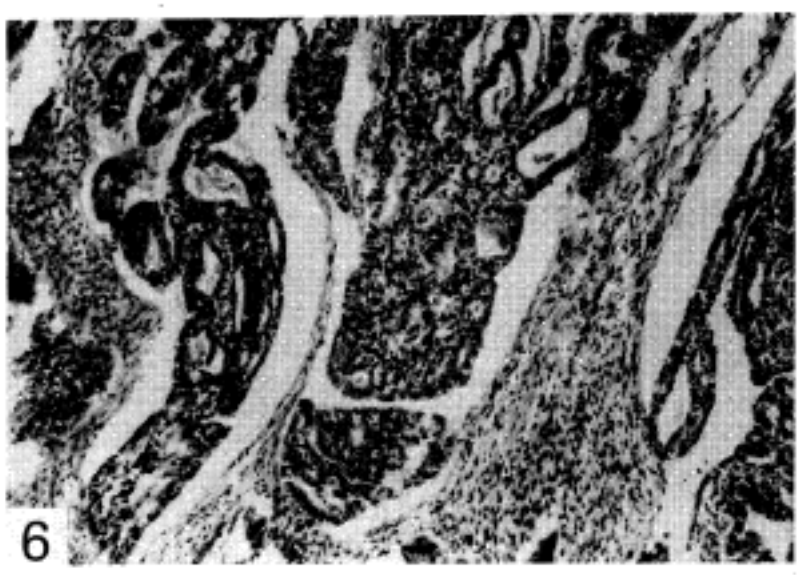

Fig. 6. Well differentiated adenocartinoma of endometrium from case 2 (H&E, ×100).

DISCUSSION

Since Stein and Leventhal[1] described a syndrome characterized by bilateral polycystic ovaries, infertility, amenorrhea, and obesity in 1935, it has been known that polycystic ovaries may be found in different clinical circumstances with normal or abnormal ovarian functions. Nowadays, this syndrome is considered to be part of spectrum of symptoms of polycystic ovary syndrome.

The principal pathologic findings in ovaries are collagenization of the superficial cortex with longstanding absence of ovulation; subcortical follicular cysts and absence of corpora lutea or albicantia. Macroscopically, the ovaries are typically rounded and usually two to four times larger than normal. Through their white surface, superficial cortical cysts are visible. On section, a thickened superficial cortex, numerous subjacent cysts, usually similar in size and less than 1 cm in diameter, and medullary stromal thickening are found. There are thick layer of luteinized theca interna cells (follicular hyperthecosis) and variable degrees of proliferation of the medullary stromal cells. Focal stromal luteinization (stromal hyperthecosis) may be seen.

The initiating factors are uncertain, but the major endocrine disturbances are disorderly released gonadotropin and excessive androgen production[2]. The resulting abnormalities are fluctuating elevated levels of luteinizing hormone and low unchanging levels of follicular stimulating hormone. Luteinizing hormone stimulates theca interna cells to produce androstenedione[2,3]. Unfortunately, in two cases, hormonal studies did not show any abnormalities.

At present time, the most popular theory about the pathogenesis of endometrial carcinoma in patients with Stein-Leventhal syndrome is the incresased production of estrone[3,4].

A number of cases of endometrial carcinoma

associated with Stein-Leventhal syndrome have been described, however, exact percentage of incidence is uncertain. According to the study of Fechner[4], the age at the time of diagnosis ranged from 16 to 40. With rare exceptions of undifferentiated carcinoma, poorly differentiated carcinoma and mixed mesodermal tumor, the endometrial carcinomas were well differentiated adenocarcinoma or adenoacanthoma. Most of the cases did not show myometrial invasion or extrauterine metastases.

In Korea, a case of endometrial carcinoma assotiated with Stein-Leventhal syndrome has been reported, which showed very similar clinical and pathologic findings as in our cases[5].

Ovarian neoplasia in polycystic ovaries included benign cystic teratoma, thecoma and arrhenoblastoma[6,7]. In one of our cases, both ovaries revealed cystadenofibroma.

Finally, it should be mentioned that the endometrial hyperplasia with or without carcinoma in premenopausal women, especially younger than age 40, should be carefully evaluated on the possibility of association with polycystic ovary syndrome.

SUMMARY

Two cases of adenocarcinoma of the endometrium associated with Stein-Leventhal syndrome in 30 and 38 years-old women were reported with brief review of literatures.

· REFERENCES

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＝국문초록＝

Stein-Leventhal 증후군에 동반된 자궁 내막 선암

—2예 보고—

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이 갑 노 · 백 승 룡

Stein-Leventhal 증후군은 지속적인 무배란과 난소의 sclerosis 때문에 나타나는 다낭성 난소 질환의 일종으로 그 빈도는 확실치 않으나 과다한 estrogen 분비로 생긴다는 것이 널리 알려져 있다. 저자들은 최근 자궁 내막의 선암이 동반된 Stein-Leventhal 증후군 2예를 경험하여 보고하는 바이다.

증례 1은 30세 여성으로 5년간의 원발성 불임, 간헐적인 무월경과 불규칙한 월경 주기를 주소로 입원하였다. 이학적 검사상 비만 이외에 특이한 소견은 없었고 비교적 여성의 2차 성징을 갖추고 있었다. 자궁소파술에서 자궁 내막의 극피세포선암으로 진단받고 자궁 적출술과 양측 부속기 절제술을 받았다.

증례 2는 38세된 여성이 원발성 불임과 간헐적인 질출혈을 주소로 입원하였다. 역시 무월경증과 불규칙한 월경주기를 호소하였다. 자궁소파술로 자궁 내막 선암으로 진단받은 후 출혈이 지속되어 재차 자궁소파술을 시행한 후 자궁 절제술과 양측 부속기 절제술을 받았다.

두 증례 모두 양측 난소의 피막은 두꺼워져 있었고 절단면상 피막하에 크고 작은 낭포들이 간질의 섬유화와 함께 관찰되었으나 황체는 없었다. 증례 1은 부분적으로 낭종성 선섬유종의 소견이 관찰되었다. 자궁 내막에서는 증례 1은 미만성 극피 세포암과 증례 2는 폴립양의 자궁 내막암이 관찰되었으며 두예 모두 자궁근내에 침윤은 없었다.