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Original Article

Histopathological Study of Endometrial Changes in Hysterectomy Specimens with Cystic Lesion of Ovary

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ABSTRACT

Introduction: Some of the ovarian lesions become functional and secrete hormones that bring endometrial changes like hyperplasias and polyps. This study aimed to find endometrial changes associated with different types of cystic lesions of the ovary.

Materials and Methods: A histopathological study done from 2010 -2013 on all the total abdominal hysterectomy specimens with bilateral oophorectomy having cyst size more than 3cms, with a detailed clinical history received in the Department of Pathology, Sri Manakula Vinayagar Medical College and Hospital, Pondicherry. A total of 112 cases were collected analyzed and statistically correlated.

Results: Out of the 112 cases of cystic lesions of the ovary 67% showed endometrium within normal limits, 33% of cystic lesions of ovary showed polyps, simple hyperplasia without atypia, complex hyperplasia without atypia. Among non-neoplastic lesions, follicular cyst produced the most endometrial changes, followed by benign surface epithelial lesions. Granulosa cell tumor was found to induce polyp as well as simple hyperplasia without atypia. Two out of three malignant lesions showed endometrial changes followed by benign lesions. The majority of the cystic lesions of the ovary encountered are non-neoplastic lesions (59%) and follicular cysts were more common (97%). Endometrial hyperplasia of both simple and complex types without atypia was found with serous cystadenoma.

Conclusions: From the current study it implicates the necessity of assessing cystic lesions of the ovary like a follicular cyst, luteal cyst, granulosa cell tumors as they can become functional leading to endometrial changes that can form a fertile ground for carcinomas.

Keywords: Cystic lesions; Endometrial hyperplasia; Ovary

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INTRODUCTION

Ovarian cysts are formed during ovulation are derived from ovarian follicles and lined by granulosa cells with an outer coat of thecal cells.[1] In some of these cysts the thecal coat becomes luteinized. Most of these cysts are clinically insignificant but some may cause hyperestrogenism. Luteal cysts are caused by failure of the involution of the corpus luteum.[2]

The ovarian tumors are classified based on the cells they arise from as surface epithelial tumors, germ cell tumors, sex cord-stromal tumors, and mesenchymal tumors. They are further divided into benign, borderline, and malignant. The tumors occurring as cystic

lesions include surface epithelium tumors, granulosa cell tumors, and teratomas.[2] The tumors arising from the sex cord-stromal tumors like granulosa cell tumors produce female hormones.[2]

Endometrium responds in various patterns, of which endometrial hyperplasia derives special attention as it is linked with endometrial carcinoma. It is divided into 2 types:

1. Simple hyperplasia with or without atypia

2. Complex hyperplasia with or without atypia

The other change that can be induced in the endometrium due to hormonal stimuli is a polyp. Most of the hyperplasia is due to excess estrogen that is due to cystic lesions of the ovary.[3] The present study is about the cystic lesions of the ovary that create a favorable environment for the changes in the uterus that includes endometrial polyp, endometrial metaplasia, and hyperplasia, which highlights the fact that the reproductive organ depends on the complex sequence of endocrinological events.

MATERIALS AND METHODS

This is a cross-sectional study done from January 2010 to December 2013 on all the total abdominal hysterectomy specimens with bilateral oophorectomy, having cystic lesions of ovary (cyst size > 3cms), with a detailed clinical history received in the Department of Pathology, Sri Manakula Vinayagar Medical College and Hospital, Pondicherry.

The specimens were fixed in 10% formalin. After adequate fixation of the specimen a brief gross description of the shape, size, color, and morphological details were entered in the per forma. The representative tissue bits were processed and routine staining was done with hematoxylin and eosin.

Inclusion criteria for the study were based on the intervention involved. 1) Only hysterectomy specimens with bilateral scalping-oophorectomy were taken. 2) Cystic ovarian lesions> 3 cms. Oophorectomy specimen or salphingo-oophorectomy specimen only, pelvic inflammatory disease specimens, and solid ovarian lesions were excluded from the study.

A total of 112 cases were collected. For the retrospective study, the clinical details collected from the Medical Record Department and the blocks were obtained from the department block collection. The study was started after the approval from the ethical clearance. Findings were recorded and the data was analyzed using Epi info program, version 7.1.4. Data were calculated with a value of significance (p-value) set at < 0.05.

RESULTS

The total number of total abdominal hysterectomy specimens with bilateral salpingo-oophorectomy was 595 out of which 112 cases were included as per inclusion criteria. The majority of the cystic lesions of the ovary showed proliferative and secretory endometrium and only 37 cases showed endometrial changes that include polyp, simple hyperplasia without atypia, complex hyperplasia without atypia.(fig. 1)

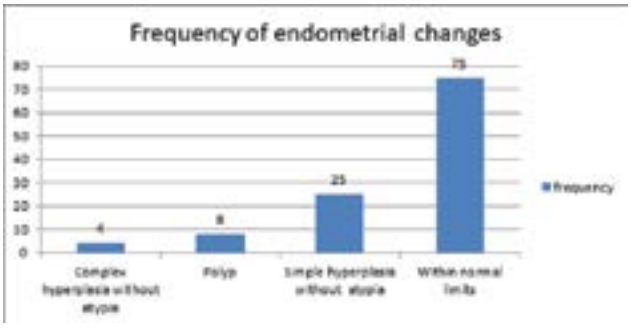

Figure 1: Frequency of endometrial changes

Out of the 112 cases, cystic lesions of the ovary 67%(75 cases) were classified as within normal physiological limits (Table 1). The majority of the nonneoplastic ovarian lesions had only proliferative and secretory endometrium. Benign ovarian cystic lesions also had similar findings.

Table 1: Endometrial changes within normal limits

Endometrial changes within normal limits	Proliferative phase	Secretory phase	Cystic atrophy
Benign	8%	10.68%	5.33%
Malignant	1.35%	-	-
Non neoplastic +benign	6.66%	6.66%	1.33%
Non neoplastic+malignant	1.33%	-	-
Non neoplastic	29.33%	29.33%	-
Total	**46.67%**	**46.67%**	**6.66%**

Among non-neoplastic ovarian cystic lesions, follicular cyst produces the most endometrial changes followed by benign surface epithelial lesions. Endometrial hyperplasia of both simple and complex types without atypia was found with serous cystadenoma. Granulosa cell tumor was found to induce polyp as well as simple endometrial hyperplasia (Table 2).

Table 2: Cystic lesions in the ovary with endometrial changes

	Cystic lesion vs. endometrial changes	Polyp	Simple hyperplasia without atypia	Complex hyperplasia without atypia	Total
Non-neoplastic	**Follicular cyst**	13.5%	40.6%	5.4%	59.5%
Benign	**Surface epithelial**	-	21.6%	2.7%	24.3%
Malignant	**Surface epithelial**	2.7%	-	-	2.7%
	Sex cord	-	2.7%	-	2.7%
	Double pathology	5.4%	2.7%	2.7%	10.8%
	Total	**21.6%**	**67.6%**	**10.8%**	**100%**

Age-wise distribution of various endooometrial changes in the study population is shown in table 3. Among the changes in the reproductive age group, simple hyperplasia was the commonest and in the postmenopausal age group, endometrial polyp and simple endometrial hyperplasia were common. However the p-value was not significant (p-value >0.05).

Table 3: Age distribution of endometrial changes

Age distribution of endometrial changes	Complex hyperplasia without atypia	Polyp	Simple hyperplasia without atypia	Within normal limits	Total
Peri menopausal	1.8%	1.8%	2.7%	17.7%	24%
Post menopausal	0	1.8%	1.8%	5.4%	9%
Reproductive	1.8%	3.6%	17.8%	43.8%	67.0%
TOTAL	**3.6%**	**7.2%**	**22.3%**	**66.9%**	**100.0%**

DISCUSSION

In the current study out of 112 cases, 67% of cystic lesions of the ovary showed endometrium at different stages of the menstrual cycle. The majority of the non-neoplastic lesions were non-functional showing only proliferative and secretory endometrium. However, these patients with nonneoplastic lesions and normal endometrium underwent hysterectomy due to abnormal uterine bleeding with no identifiable lesions.

Any bleeding not due to bleeding from the secretory endometrium associated with anovulatory cycle not exceeding a length of 5 days is termed as abnormal uterine bleeding.[3] Some of them have identifiable causes like an endometrial polyp or submucous myoma, or in postmenopausal bleeders cancer or atrophic endometrium, degenerative changes in uterine blood vessels.[4-6]In the current study, 33% of cases showed endometrial changes that had identifiable lesions such as polyps and hyperplasias mostly due to functional cystic ovarian lesions.

Bleeding not associated with an organic cause in women mostly of reproductive age group belong to dysfunctional uterine bleeding of two categories one associated with ovulation and more numerous in which ovulation has not occurred. In ovulatory bleeding can be due to inadequate proliferative phase, inadequate secretory phase, or irregular shedding of the endometrium. Anovulatory cycle can be recognized by finding a proliferative endometrium at a time of the cycle when a secretory pattern is expected mostly during unremitting estrogen stimulation that results in endometrial hyperplasia.[3]

In the current study, 33% of cases showed endometrial changes among which the non-neoplastic that includes follicular cyst and luteal cyst showed 59.5% of endometrial changes in the form of polyp and hyperplasia. Follicular and luteal cysts when persistent are associated with manifestations of excess estrogen production that leads to irregular menses or endometrial hyperplasias in women of reproductive age.[1]

From various studies that solitary follicular cysts are common soon after menarche and around the time of menopause, they can also be encountered at any age from the fetal period to 7 years after the clinical onset of menopause.[7-11]Corpus luteal cyst can occur during reproductive years and also isolated cases can occur after the clinical onset of menopause. The follicular cysts may be incidental findings or may be due to palpable adnexal masses or manifestations due to increased estrogen production, menstrual disturbances, or endometrial hyperplasia.[12]

In the current study, most of the granulosa cell tumor showed endometrial hyperplasia in the form of SH and a polyp in the double pathology category with a follicular cyst and granulosa cell tumor. Only 1.33% of the malignant lesion was non-functional majority showed endometrial changes like hyperplasia and polyp.

Adult granulosa cell tumors are the most common ovarian tumor, associated with estrogenic manifestations because of the estrogen production the patients are at up to 50% concurrent risk of endometrial hyperplasia and 10% risk of adenocarcinoma.[1] Various studies show that granulosa cell tumor is associated with hyperestrinism in three fourth of the cases that lead to metrorrhagia in adults including postmenopausal patients .[13]

Granulosa cell tumors produce a variety of steroid hormones, when functional most are estrogenic. In women of reproductive age, the tumor may be associated with a variety of menstrual disorders related to hyperoestrinism.In postmenopausal women, irregular uterine bleeding due to various types of endometrial hyperplasia or rarely well-differentiated adenocarcinoma is the most common manifestation of hyperoestrinism.[14]

Granulosa cell tumors account for approximately 1.5% of all ovarian neoplasms and 6% of ovarian cancers.[15-17] Approximately 75% are estrogenic causing endometrial changes and some are androgenic.[18]

In the current study majority of endometrial changes occurred in the reproductive age group, SH was the commonest and in the postmenopausal age group, polyp and SH both were common. CH was observed in 10.8% of cases of which 5.4% belonged to nonneoplastic follicular cyst and 2.7% to the serous surface epithelial lesion and 2.7% to the mixed lesions. The majority of endometrial changes were seen in non-neoplastic lesions, two out of three malignant lesions showed endometrial changes followed by benign lesions.

As seen in the current study endometrial hyperplasias occur frequently in cases with unopposed estrogen sources both endogenous or exogenous such as estrogen secreting ovarian neoplasms and successive prolonged periods of ovulation .[1]

From various studies, endometrial hyperplasias occur in the peri and post-menopausal years and rare instances show signs of atypical hyperplasias.[19] Most of them are due to normal endometrial response to sustained estrogen levels unrelieved by progesterone and endometrial polyps are characteristically aymptomatic, incidental findings are seen in perimenopausal women as they cause clinically significant bleeding or spotting.[12]

Women with ovarian estrogen secreting tumors have a higher risk of developing endometrial cancer as prolonged estrogen stimulation leads to endometrial hyperplasia partly explains why there is an increased risk of endometrial cancer.[20]

A study done by Areene et al [21] states that type 1 endometroid carcinomas arising from atypical complex hyperplasias affects peri and postmenopausal women and are usually associated with estrogen receptor-positive tumors associated with hyperestrogenism and estrogen stimulation due to various causes like obesity, diabetes, high blood pressure, breast cancer, chronic anovulation, estrogen-producing ovarian tumors, and genetic predisposition [23-25] In contrast, type II endometrial [22] carcinoma does not have the predisposition as in Type 1.

From the current study, it implicates the necessity of assessing cystic lesions of the ovary based on size, laterality, and age group as some of the cystic lesions of the ovary like a follicular cyst, luteal cyst, granulosa cell tumors can become functional leading to endometrial changes that can form a fertile ground for carcinomas.

CONCLUSIONS

The majority of ovarian cystic lesions revealed endometrium at different stages of menstrual endometrium. The majority of the non-neoplastic lesions were non-functional showing only proliferative and secretory endometrium. However, some cystic ovarian lesions tend to have simple endometrial hyperplasia, hyperplasia with atypia. It is more common among neoplastic lesions of the ovary. Hence in neoplastic ovarian lesions, endometrial pathology has to be looked for.

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