IJPRP

Indian Journal of Pathology: Research and Practice
Volume 9 Number 1 (Part II), January - April 2020
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.9120.22

Original Research Article

Histopathological Study of Endometrium and Ovary in Hysterectomy with Salphingo-oophorectomy Specimens

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Received on 01.02.2020

Accepted on 02.03.2020

Abstract

Introduction: Endometrium being a dynamic tissue undergoes physiologic and morphologic changes in response to hormones produced in ovary. Various patterns of subtle ovarian changes is related to morphologic alterations in endometrium. *Objective:* To correlate histopathological features of endometrium with those of ovarian pathology in hysterectomy with salphingo-oophorectomy specimens. *Materials and methods:* It was a retrospective study of hysterectomy with salpingo-oophorectomy specimens from January 2017 to June 2018. Histopathology slides were reviewed and findings were documented. Various histopathological patterns in endometrium and corresponding ovarian histopathological features were documented, categorized and analyzed. *Results:* One hundred and forty-three cases were analyzed. Endometrium showed proliferative phase in 47 cases (32.87%) and constituted the most common pattern. Right ovary was examined in 134 cases. Left ovary was examined in 114 cases. Both the ovaries showed corpus albicans as the most common non-neoplastic finding. Right ovary showed benign serous cystadenoma [3.73%] as the most common neoplastic lesion. Left ovary showed benign cystic teratoma [2.63%] as the most common neoplastic lesion. *Conclusion:* Histopathological changes in ovary and endometrium are complimentary. Ovarian tissue findings may reflect histopathological patterns of endometrium.

Keywords: Hormones; Cystadenoma; Teratoma.

How to cite this article:

G Noor Afshan, Ramaswamy AS, BN Kumarguru, et al. Histopathological Study of Endometrium and Ovary in Hysterectomy with Salphingo-oophorectomy Specimens. Indian J Pathol Res Pract.2020;9(1 Part II):146-155.

Introduction

Endometrium is a dynamic tissue. It undergoes physiologic and morphologic changes during the menstrual cycle in response to sex-steroid hormones produced in the ovary. This is in turn is under the effect of hormones produced by pituitary and hypothalamus. Disturbance in the pituitary-hypothalamus-ovarian axis results in abnormal uterine bleeding. Abnormal uterine bleeding (AUB) is a debilitating condition and most common complaint constituting 33% of gynecological referrals. It affects 14–25% of women in the reproductive age and 69% in perimenopausal and postmenopausal women.[1] Both dysfunctional uterine bleeding and erratic bleeding due to hormonal disturbances, structural

causes due to fibroids, polyps, carcinomas and infections comprise the various etiological factors of abnormal uterine bleeding.[2] The various patterns of subtle ovarian changes is related to the various morphological alterations of endometrial glands and stroma.[3] The current study was undertaken to correlate histopathological features of endometrium with those of co-existing ovarian pathology in hysterectomy with salphingo-oophorectomy specimens.

Materials and Methods

The study was conducted in the department of Pathology from January 2017 to June 2018 for a period of eighteen months. It was a retrospective observational type of study. The study was approved by Institutional Ethics committee. Study population constituted female patients who underwent hysterectomy with salpingo-oophorectomy.

One hundred and forty-three cases were analyzed. All cases in which hysterectomy with salpingo-oophorectomy was performed were included in the study. Those cases in which only endometrial biopsies and only hysterectomy specimens were received were excluded from the study. Histopathology request forms were retrieved. Available clinical details were collected and documented. Histopathology slides of the cases stained by hematoxylin and eosin (H&E) were retrieved and examined. Various histopathological patterns in the endometrium and the corresponding ovarian histopathological features were documented and categorized. Grading and categorization were applied for neoplastic lesions according to 2014 WHO [World Health Organization] classification. Histopathological findings of endometrial tissue was compared and correlated with those of ovarian tissue.

Results

A total of one hundred and forty-three cases were analyzed. Majority cases of cases were seen in the fifth decade constituting 80 cases (55.94%). Evaluation of endometrium revealed various patterns of endometrial changes. The most common pattern seen was proliferative endometrium [44 cases (30.77%)] followed by secretory endometrium [39 cases(27.27%)]. Right ovary was examined in 134 cases and the left ovary was examined in 114 cases. Evaluation of both ovaries revealed follicular cyst as the most common non-neoplastic lesion. Right ovary showed benign serous cystadenoma [5 cases (3.73%)] as the most common neoplastic lesion. Left ovary showed benign cystic teratoma [3 cases (2.63%)] as the most common neoplastic lesion.

In proliferative phase, the most common finding documented in both ovaries was corpus albicans followed by follicular cyst. In disordered proliferative phase, the most common finding documented was hemorrhagic corpus luteum [7 cases (36.84%)] in right ovary and follicular cyst [6 cases (31.58%)] in left ovary. In secretory phase, the most common finding observed in both ovaries was corpus albicans followed by hemorrhagic corpus luteum [12 cases (30.77%)] in right ovary and follicular cyst [8 cases (20.51%)] in left ovary. In atrophic endometrium and atrophic endometrium with chronic endometritis, corpus albicans was the most common finding documented in both ovaries. In chronic endometritis, corpus albicans was the most common finding documented in both ovaries, followed by cystic follicle [3 cases (37.5%)) in the right ovary and follicular cyst [2 cases (25%)] in the left ovary. In pill endometrium, corpus albicans was the most common finding documented in both ovaries followed by cortical inclusion cyst [2 cases (40%) in right ovary. Left ovary showed cystic follicle [2 cases (40%)] and follicular cyst [2 cases (40%)]. In endometrial polyps, the most common finding documented was corpus albicans. In non-atypical hyperplasia, the most common finding documented in the right ovary was corpus albicans [5 cases (71.42%)] followed by follicular cyst [1 case (14.28%)] and benign cystic teratoma [1 case (14.28%)]. The most common finding documented in the left ovary was cortical inclusion cyst [2 cases (28.57%). In endometrioid carcinoma, the common

Table 1: Histopathological findings in endometrium and ovary

Histopathogical findings in endometrial tissue	
Endometrial phases and Non-neoplastic lesion	**Cases (%)**
Proliferative endometrium	44 (30.77%)
Secretory endometrium	39 (27.27%)
Disordered proliferative endometrium	19 (13.29%)
Atrophic endometrium	9 (6.29%)

Chronic endometritis	8 (5.59%)
Pill endometrium	5 (3.50%)
Atrophic endometrium with chronic endometritis	1 (0.70%)
Neoplastic endometrial lesions	
Endometrial polyp	9 (6.29%)
Non-atypical hyperplasia	7 (4.90%)
Endometrioid carcinoma	2 (1.40%)

Histopathogical findings in ovarian tissue		
Ovary	**Right ovary cases (%)**	**Left ovary cases (%)**
Non-neoplastic lesions		
Corpus albicans*	87 (64.92%)	76 (66.67%)
Follicular cyst	28 (20.89%)	26 (22.8%)
Hemorrhagic corpus luteum	22 (16.41%)	6 (5.26%)
Cystic follicle	21 (15.67%)	14 (12.28%)
Corpus luteum	14 (10.44%)	7 (6.14%)
Cortical inclusion cyst	8 (5.97%)	8 (7.01%)
Corpus luteum cyst	3 (2.23%)	3 (2.63%)
Endometriosis	1 (0.74%)	1 (0.87%)
Stromal hyperplasia	–	1 (0.87%)
Transitional cell rests	–	1 (0.87%)
Neoplastic lesions		
Benign serous cystadenoma	5 (3.73%)	2 (1.75%)
Benign mucinous cystadenoma	3 (2.2%)	1 (0.87%)
Benign cystic teratoma	2 (1.49%)	3 (2.63%)
Benign sero-mucinous cystadenoma	2 (1.49%)	1 (0.87%)
Benign Brenner	1 (0.74%)	1 (0.87%)
Mucinous cystadenocarcinoma	1 (0.74%)	1 (0.87%)
Granulosa cell tumor	1 (0.74%)	1 (0.87%)
Benign serous cystadenofibroma	–	1 (0.87%)

* No other significant pathology

Table 2: Histopathological findings of ovary in different phases of endometrium and non-neoplastic endometrial lesions

Ovarian changes	**Right ovary Cases (%)**	**Left ovary Cases (%)**
Proliferative Phase (*n* = 44)		
Corpus albicans*	30 (68.18%)	33 (75%)
Follicular cyst	10 (22.72%)	7 (15.9%)
Cystic follicle	5 (11.36%)	3 (6.81%)
Cortical inclusion cyst	3 (6.81%)	2 (4.54%)
Benign serous cystadenoma	–	1 (2.27%)
Benign mucinous cystadenoma	1 (2.27%)	–
Benign sero-mucinous cystadenoma	1 (2.27%)	1 (2.27%)
Adult granulosa cell tumor	1 (2.27%)	–
Benign Brenner tumor	1 (2.27%)	1 (2.27%)
Stromal hyperplasia	–	1 (2.27%)
Transitional cell rest	–	1 (2.27%)
Benign cystic teratoma	–	1 (2.27%)
Disordered Proliferation (n=19)		
Hemorrhagic corpus luteum	7 (36.84%)	–
Corpus albicans*	6 (31.58%)	4 (21.05%)
Corpus luteum	3 (15.79%)	1 (5.26%)
Cystic follicle	3 (15.79%)	5 (26.32%)
Follicular cyst	3 (15.79%)	6 (31.58%)
Corpus luteal cyst	2 (10.53%)	2 (10.53%)
Benign serous cystadenoma	2 (10.53%)	–

Ovarian changes	Right ovary Cases (%)	Left ovary Cases (%)
Benign sero- mucinous cystadenoma	1 (5.26%)	–
Cortical inclusion cyst	–	1 (5.26%)
Secretory Phase (n=39)		
Corpus albicans*	22 (56.41%)	23 (58.97%)
Hemorrhagic corpus luteum	12 (30.77%)	4 (10.25%)
Follicular cyst	9 (23.07%)	8 (20.51%)
Corpus luteum	9 (23.07%)	6 (15.38%)
Cystic follicle	5 (12.82%)	5 (12.82%)
Corpus luteal cyst	1 (2.56%)	1 (2.56%)
Cortical inclusion cyst	1 (2.56%)	1 (2.56%)
Benign serous cystadenofibroma	–	1 (2.56%)
Benign cystic teratoma	–	1 (2.56%)
Atrophic Endometrium (*n* =9)		
Corpus albicans*	4 (44.40%)	4 (44.40%)
Mucinous cystadenoma	2 (22.20%)	–
Benign serous cystadenoma	2 (22.20%)	1 (11.10%)
Follicular cyst	1 (11.10%)	–
Cortical inclusion cyst	1 (11.10%)	–
Endometriosis	–	1 (11.10%)
Atrophic Endometrium With Chronic Endometritis (*n* = 1)		
Corpus albicans*	1 (100%)	1 (100%)
Chronic Endometritis (n=8)		
Corpus albicans*	6 (75%)	5 (62.50%)
Cystic follicle	3 (37.50%)	–
Follicular cyst	2 (25%)	2 (25%)
Hemorrhagic corpus luteum	1 (12.50%)	–
Cortical inclusion cyst	1 (12.50%)	1 (12.50%)
Endometriosis	1 (12.50%)	–
Pill Endometrium (n=5)		
Corpus albicans*	3 (60%)	2 (40%)
Cortical inclusion cyst	2 (40%)	1 (20%)
Corpus luteum	1 (20%)	–
Hemorrhagic corpus luteum	1 (20%)	–
Cystic follicle	1 (20%)	2 (40%)

*No other significant pathology

Table 3: Histopathological findings of ovary in neoplastic endometrial lesions

Ovarian changes	Right ovary Number (%)	Left ovary Number (%)
Endometrial Polyp (n=9)		
Corpus albicans*	6 (66.67%)	4 (44.44%)
Corpus luteum	1 (11.10%)	–
Hemorrhagic corpus luteum	1 (11.10%)	–
Cystic follicle	1 (11.10%)	–
Follicular cyst	1 (11.10%)	–
Benign serous cystadenoma	1 (11.10%)	–
Mucinous cystadenocarcinoma	1 (11.10%)	1 (11.10%)
Granulosa cell tumor	–	1 (11.10%)
Non-Atypical Hyperplasia (n=7)		
Corpus albicans*	5 (71.42%)	–
Follicular cyst	1 (14.28%)	–
Benign cystic teratoma	1 (14.28%)	–
Cystic follicle	–	1 (14.28%)
Cortical inclusion cyst	–	2 (28.57%)

Ovarian changes	Right ovary Number (%)	Left ovary Number (%)
Endometrial carcinoma (n=2)		
Corpus albicans*	2 (100%)	2 (100%)

*No other significant pathology

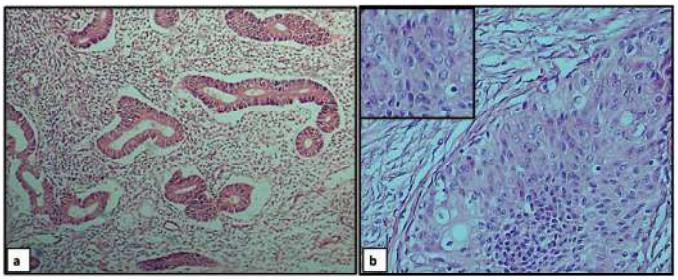

Fig. 1a-b: (a) Microphotograph of tissue section of endometrium in proliferative phase- displaying proliferative endometrial glands. [H&E, X400]. (b) Microphotograph of tissue section of ovarian tissue of corresponding case displaying Brunner tumor. Inset: Tumor cells showing nuclear grooves. [H&E, X400].

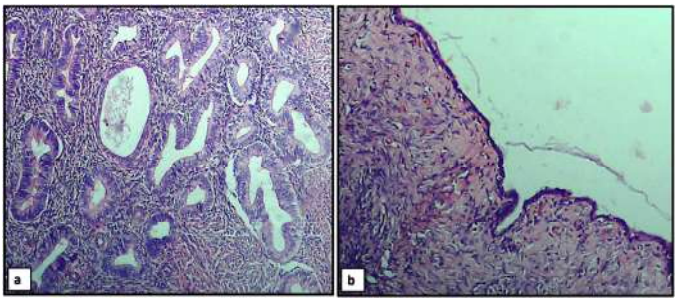

Fig. 2a-b: (a) Microphotograph of tissue section of endometrium displaying disordered proliferation. [H&E, X400]. (b) Microphotograph of tissue section of ovarian tissue of corresponding case displaying Benign serous cystadenoma. [H&E, X400].

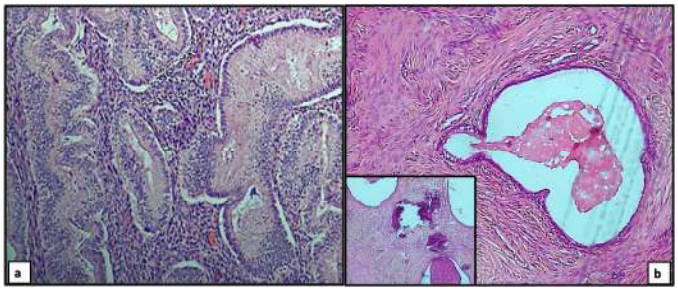

Fig. 3a-b: (a) Microphotograph of tissue section of endometrium in secretory phase- displaying tortuous endometrial glands. [H&E, X400]. (b) Microphotograph of tissue section of ovarian tissue of corresponding case displaying Sero-mucinous cystadenofibroma. Inset: Calcification. [H&E, X400].

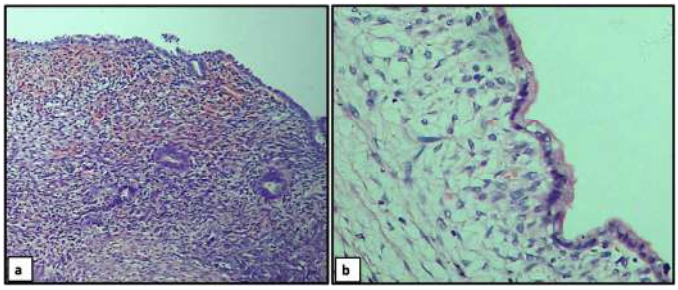

Fig. 4a-b: (a). Microphotograph of tissue section of atropic endometrium - displaying atrophic endometrial glands. [H&E, X400]. (b) Microphotograph of tissue section of ovarian tissue of corresponding case displaying mucinous cystadenoma. [H&E, X400].

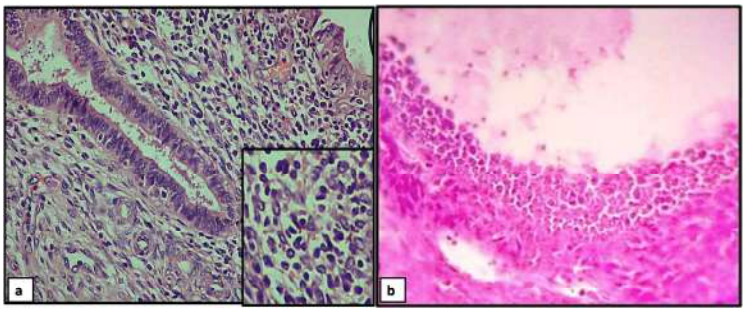

Fig. 5a-b: (a) Microphotograph of tissue section of chronic endometritis- displaying endometrial glands and chronic inflammatory cell infiltration. Inset: lymphocytic & plasma cell infiltration [H&E, X400]. (b) Microphotograph of tissue section of ovarian tissue of corresponding case displaying follicular cyst. [H&E, X400].

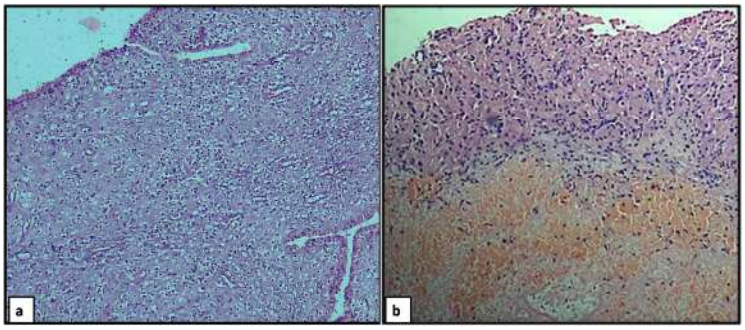

Fig. 6a-b: (a) Microphotograph of tissue section of pill endometrium - displaying atrophic endometrial glands and decidualized stroma. [H&E, X400]. (b) Microphotograph of tissue section of ovarian tissue of corresponding case displaying corpus haemorrhagicum. [H&E, X400].

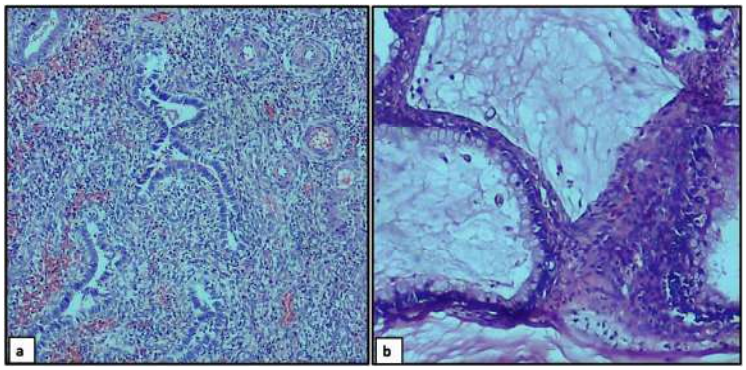

Fig. 7a-b: (a) Microphotograph of tissue section of endometrial polyp- displaying proliferative phase endometrial glands and thickened blood vessels. [H&E, X400]. (b) Microphotograph of tissue section of ovarian tissue of corresponding case displaying mucinous cystadenocarcinoma. [H&E, X400].

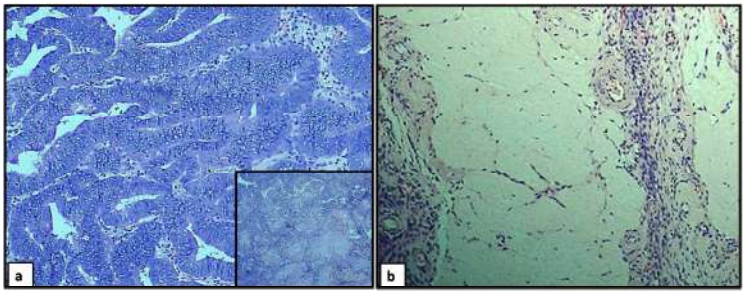

Fig. 8a-b: (a)Microphotograph of tissue section of endometrioid carcinoma- displaying closely packed malignant endometrial glands arranged in back to back fashion. Inset: squamous morules [H&E, X400]. (b) Microphotograph of tissue section of ovarian tissue of corresponding case displaying corpus albicans. [H&E, X400].

finding documented in both ovaries was corpus albicans.

Figs 1-8 are microphotographs showing various endometrial lesions and ovarian lesions of the corresponding cases.

Discussion

Endometrium is a hormonally sensitive and responsive tissue which constantly and rhythmically undergoes structural reorganization with each menstrual cycle in preparation for implantation process. In the absence of implantation, superficial layer is partially or completely shed and remodeled in preparation for the next cycle. Estrogen and progesterone are hormones secreted by the ovarian tissue necessary for implantation and maintaining the integrity.[4,5]

The distribution of various endometrial patterns and ovarian findings in the present study were compared with other studies. In the present study, clustering of the cases was observed in fifth decade. Sandhya M et al[2] and Rather GR et al.[6] had observed that majority of the cases was seen in fifth decade in their study. In contrast, Supriya M et al.[1] documented majority of the cases in third decade and Dayal S et al.[4] documented majority of the cases in the fourth decade.

Histopathological examination of endometrium revealed a variety of patterns. Proliferative phase [44 cases (30.77%)] was found to be the predominant pattern followed by secretory phase [39 cases (27.27%)]. Similar findings were observed in the study conducted by Sandhya M et al.[2] and Dayal S et al.[4] Verma D et al.[7] had documented proliferative phase as the most common pattern followed by atrophic endometrium. In contrast, Vaidya S et al.[8] documented secretory phase as the predominant pattern followed by proliferative phase. Supriya et al.[1] documented also documented endometrial hyperplasia with majority of cases in the perimenopausal age group as the most common organic cause in their study. Rather GR et al[6] documented normal histology (83.09%) as the commonest endometrial pattern followed by atrophic endometritis in their study. However the author had not specified the pattern of normal histology (proliferative phase or secretory phase). Endometrioid carcinoma was the least common finding in the present study. Sandhya M et al.[2] had also documented endometrial carcinoma in their study (Table 4).

Table 4: Comparison of endometrial finding in various studies

Histopathological findings	Authors						
	Supriya M et al.[1] (2017, India)	Sandhya M et al.[2] (2017, India)	Dayal S et al.[4] (2016, India)	Verma D et al.[7] (2016, India)	Vaidya S et al.[8] (2013, Nepal)	Rather GR et al.[6] (2013, India)	Present study (2018, India)
Proliferative phase	11.49%	48.43%	48.57%	53%	18.36%	_	30.77%
Secretory phase	2.2%	15.42%	29.46%	–	22.58%	_	27.27%
Disordered proliferative phase	5.74%	–	–	–	13.40%	1.14%	13.29%
Non-atypical hyperplasia	57.47%	4.57%	5.03%	12%	10.92%	3.29%	4.90%
Atrophic Endometrium	–	14.69%	14.18%	31%	4.71%	5.44%	6.29%
Endometrial Polyp	28.57%	1.68%	1.83%		1.24%	2.43%	6.29%
Chronic endometritis	_	0.72%	2.28%	_	_	1.57%	5.59%
Pill endometrium	_	0.24%	_	_	6.20%	_	3.50%
Endometrioid carcinoma	_	1.44%	–	–	–		1.40%
Total cases	87	415	437	152	403	698	143

Histopathological examination of the ovary also revealed a variety of findings. Follicular cyst [28 cases (20.89%)] was the most common non-neoplastic lesion observed in the present study. Rather G et al.[6] and Verma D et al.[7] documented similar observation in their studies. Follicular cyst (44.2%) was the predominant ovarian lesion associated with endometrial hyperplasia and endometrial carcinoma in a study conducted by Rao S et al.[9] In contrast, Dayal S et al.[4] found corpus

luteal cyst as the commonest non -neoplastic lesion in their study. Endometriosis [1 case (0.74%)] was the least common non-neoplastic lesion in the present study. Rather G et al.[6] also documented similar observation in their study.

Benign serous cystadenoma [5 cases (3.73%)] was the most common neoplastic lesion observed in the present study. Verma D et al.[7] also documented similar findings in their study. In contrast, Rather G et al.[6] documented benign mucinous cystadenoma

Table 5: Comparison of ovarian findings in various studies

Histopathological Features	Authors			
	Dayal S et al.[4] (2016, India)	Verma D et al.[7] (2016, India)	Rather GR et al.[6] (2013, India)	Present study (2018, India)
Non- neoplastic				
Corpus luteal cyst	4.34%	8%	16.34%	2.23%
Hemorrhagic corpus luteum				16.41%
Follicular cyst	0.91%	64%	27.52%	20.89%
Cortical inclusion cyst			0.41%	5.97%
Cystic follicle				15.67%
Endometriosis			0.41%	0.74%
Neoplastic				
Benign cystic teratoma	0.45%	3%	0.41%	1.49%
Benign Brenner tumor				0.74%
Benign serous cystadenoma	0.22%	7%	1.02%	3.73%
Benign mucinous cystadenoma		1%	1.44%	2.2%
Benign seromucinous cystadenoma				1.49%
Mucinous cystadenocarcinoma				0.74%
Granulosa cell tumor			0.20%	0.74%
Total cases	437	152	658	143

as the most common neoplastic lesion and Dayal S et al.[4] documented dermoid cyst as the most common neoplastic lesion in their study (Table 5)

In normal cycles, menstrual shedding of endometrium is followed by endometrial proliferation under the influence of estrogen hormone produced by ovary in the intial phase of the menstrual cycle. Secretory phase is the second half of menstrual cycle characterized by endometrial proliferation, wall thickening of vessels, coiling of endometrial glands and spiral arterioles formation under the influence of estrogen and progesterone.[5] Disordered proliferative endometrium is a focal process without an increase in the endometrial volume and cannot be dated to any specific time of menstrual cycle. The entity is not abnormal enough to be considered hyperplastic.[10] Even in the present study, ovarian tissue showed varied morphological finding in cases of disorded proliferative endometrium.

The exact etiology of bleeding in atrophic endometrium is not known. It has been thought to be due to anatomic vascular variations or local hemostatic mechanisms or prolonged absence of any exogeneous or endogeneous estrogenic stimulation.[5,8]

Endometrial hyperplasia is a common cause for abnormal bleeding in the perimenopausal group.[5] It is often seen in climacteric period due to anovulatory cycles. Transition of ovarian function is evidenced by pronounced fluctuation of oestrogen production. These results from either excessive endogenous production or exogenous administration of estrogens.[11] Besides hyperplasia, prolonged estrogen stimulation leading to development of polyps and endometrioid adenocarcinomas (Type I).[5,11]

One of the major reasons of excess endogenous estrogen production is estrogen secreting ovarian lesions which could be either neoplastic or non-neoplastic ovarian lesions. Follicular cyst results due to distension of developing atretic follicles. They are usually asymptomatic and can occur at any age from infancy to menopause. The presence of follicular cyst with endometrial hyperplasia or carcinoma suggests a direct relationship with hypoestrogenic state.[9]

The link between ovulatory cycles, endometrial and ovarian cancer shows the potential relevance of consideration of risk factors to molecular pathogenesis. Incessant ovulation correlates with incessant menstruation which involves

repeated disruption and re-growth of the uterine lining. Greater number of cycles of endometrial regeneration increases the likelihood of random genetic mutations because DNA replication errors occur during cell division. Thus, cancer is more likely to occur in tissues undergoing many cell divisions. In endometrial cancer, MSI occurs most commonly from epigenetic silencing and inactivation of the mutL homolog 1 (MLH1) gene through hypermethylation of CpG islands in its promoter region.[12]

For ovarian cancer, monthly disruption and repair of the surface epithelium of the ovary is proposed to lead to genetic damage, due to the accumulation of mutations of p53 tumor suppressor in the ovarian or tubal epithelium.[12–14] Germ line mutation involving BRCA1 and BRCA 2 genes predispose to 10% of ovarian cancers.[15] Mutation in KRAS, BRAF and PTEN are seen in mucinous, endometrioid and low-grade serous cancers and these may originate from ovarian cortical inclusion cysts.[13]

Most of the studies have described endometrium and ovarian pathology separately. But association had not been analyzed. The present study highlights the pattern of various ovarian lesions that can occur in a particular setting of endometrial lesion. Histopathological correlation of endometrial and ovarian lesions would help us to understand the disease process better.

Limitations

Number of cases in present study was relatively less in comparison to the other studies. The treatment history (exact nature of medication) was not available in many of the cases. Hence exact clinical correlation was difficult. In the cases in which, only unilateral salphingo-oophorectomy was performed, the pathology in the other ovary was unknown and could not be determined. It may be suggested that future studies may be done on bilateral salphingo-oophorectomies and may be correlated with treatment history.

Conclusion

Histopathological changes in ovary and endometrium are complimentary. Ovarian tissue changes may reflect the histopathological patterns of endometrium. Histopathological correlation of endometrial and ovarian lesions would help us to understand the disease process better.

Acknowledgement

We sincerely thank the histopathology technicians, Department of Pathology for the kind co-operation extended to us for the work up of the cases during the course of the study.

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