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A clinicopathological study of ovarian endometriotic cysts

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ABSTRACT

Introduction: Endometriosis is an important gynecologic disorder with multifactorial causes, primarily affecting women during their reproductive years. Pathologically, it is the result of functional endometrium located outside the uterus which may vary from microscopic endometriotic implants to large cysts. Endometriotic cysts and infertility is a well-known association. Some patients are asymptomatic while others present with disabling pelvic pain, infertility, or adnexal masses. Cyst aspiration, fenestration and ablation of cyst wall are commonly performed surgical procedures. Excision of the cyst wall is an accepted surgical treatment owing to the low recurrence rates.

Materials and Methods: A total of 35 patients who underwent ovarian cystectomy for endometriotic cysts between January 2019 and December 2020 were retrospectively identified. The clinical findings, gross and histopathological features were noted in each case. Microscopically, the presence or absence of ovarian tissue adjacent to the cyst wall was evaluated. If ovarian tissue was present, the morphologic characteristics were graded on a semi-quantitative scale of 0-4 as described by Muzii et al.

Results: The age group of patients ranged between 22-28yrs. Right side cysts accounted for the majority, however 6 cases had bilateral endometriotic cysts. Majority of patients presented with primary infertility (46.2%). The maximum weight recorded for these cysts was 35gm, size ranging between 4.5 to 18cm and median thickness of the cyst wall being 0.7cm. 68% of the cysts showed a lining epithelium, few showing atypia and oncocyctic change. Fibrosis and hemosiderin laden macrophages were present in more than 70% of cases and endometrial glands and stroma in more than 50%. Inflammation when present was predominantly lymphocytic. On evaluation of the ovarian tissue, 42.8% of cases showed no follicles and the rest showing grades ranging from 1 to 4, with grade 1 accounting for majority.

Conclusion: The present study further emphasizes endometriosis to be an important cause of primary infertility which needs to be recognized and treated appropriately. Recognition of these cysts on histopathological examination can be challenging at times when endometrial stroma is scant and in cases of tubo-ovarian masses where these lesions could mimic malignancy. The excision of endometriotic cyst wall may cause loss of functional ovarian tissue in patients with primary infertility and thus could effect the response to ovarian stimulation, oocyte recovery, implantation and fertilization rates in these patients.

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1. Introduction

Endometriosis is an important gynecologic disorder with multifactorial causes, primarily affecting women during

their reproductive years. It usually affects premenopausal females.^{1,2} Pathologically, endometriosis refers to the presence of functioning endometrial glands and stroma outside the uterine cavity, which may vary from microscopic endometriotic implants to large cysts.²⁻⁴ The various sites where these can be found include both the ovaries,

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the pouch of Douglas, pelvic peritoneum and uterosacral ligaments.^{4,5} Clinically patients may be asymptomatic or may present with disabling pelvic pain, infertility, or adnexal masses.^{1,5,6} Occasionally these can enlarge to present as huge abdominal masses which can mimic ovarian malignancy. Cyst aspiration, fenestration and ablation of cyst wall are some the commonly performed surgical procedures.^{7,8}

2. Materials and Methods

A total of 35 patients who underwent ovarian cystectomy for endometriotic cysts between January 2019 and December 2020 were retrospectively identified. The clinical findings, gross and histopathological features were noted in each case. Microscopically, all the histopathological features were noted and the presence or absence of ovarian tissue adjacent to the cyst wall was evaluated. If ovarian tissue was present, the morphologic characteristics were graded on a semi-quantitative scale of 0-4 as described by Muzii et al.⁴ Grade 0: complete absence of follicles; Grade 1: primordial follicles only; Grade 2: primordial and primary follicles; Grade 3: some secondary follicles; Grade 4: pattern of primary and secondary follicles as seen in the normal ovary.

3. Results

The age group of patients ranged between 22-28yrs. Right side cysts accounted for the majority, however 6 cases had bilateral endometriotic cysts.

Clinically patients presented with primary infertility, pain abdomen, dysmenorrhea and dyspareunia. A combination of these clinical features were frequently found. However those with primary infertility accounted for the majority accounting for 46.2%.

Table 1: Graph showing the various clinical features

Clinical feature	Percentage
Primary infertility	46.2%
Pain abdomen	38%
Dysmenorrhoea	42.8%
Dyspareunia	32%

On gross morphological examination, the maximum weight recorded for these cysts was 35gm. The size of the lesions ranged from 4.5 to 18cm with the median thickness of the cyst wall being 0.7cm. More than 80% of the cases presented as cystic lesions filled with chocolate coloured thick fluid.

Table 2: Gross morphological features of the cysts analysed

Gross Morphological Features		
Weight range	5gm	35gm
Size	4.5cm	18cm
Median wall thickness	0.7cm	

On analysis of the various histopathological features, the lining epithelium was identified in about 68% of cases, few showing atypia and oncocyctic change. (3.9% and 4.3%). Fibrosis and hemosiderin laden macrophages were present in 72.6% and 80.6% of cases respectively. Endometrial glands and stroma were present in 53.2% and 61% cases respectively. Inflammation when present was predominantly lymphocytic. [Figures 1, 2, 3, 4, 5 and 6]

Table 3: Histopathological features of endometriotic cysts analysed

Features analysed	Present (%)
Lining Epithelium	68%
Present with atypia	3.9%
Oncocyctic change	4.3%
Fibrosis	72.6%
Adjacent endometrial glands	53.2%
Endometrial stroma	61%
Hemosiderin laden macrophages	80.6%
Ceroid laden macrophages	6.8%
Inflammatory Component	
Lymphocytes	59.2%
Plasma cells	43%
Eosinophils	2.3%
Neutrophils	5.5%
Histiocytes	96.7%

On evaluation of the ovarian tissue, 42.8% of cases showed no follicles and the rest showing grades ranging from 1 to 4, with grade 1 accounting for majority.

Table 4: Grading of adjacent ovarian tissue in endometriotic cysts

Grade	No of cases (Frequency)	Percentage
0	15	42.8
1	8	22.8
2	4	11.5
3	6	17.2
4	2	5.7
Total	35	100

4. Discussion

In 1957 Hughesdon demonstrated that 93% of ovarian endometriotic cysts are formed by invagination of the cortex after the accumulation of menstrual debris from endometriotic implants.^{1,6,9} However in 1997 Nisolle and Donnez suggested that coelomic metaplasia of the invaginated epithelial inclusion is responsible. Scurrey J et al. in 2001 has described the various types of ovarian endometriotic cysts.^{3,4,10} [Table 5]

In the present study, majority of patients presented with primary infertility, accounting for 46.2%. Several authors have described various biological mechanisms that link infertility and endometriosis. Endometriosis can cause

Table 5: Pathogenetic types of endometriotic cysts.

Cortical invagination cysts	Surface inclusion cyst-related endometriotic cysts	Physiological cyst-related endometriotic cysts
They arise when surface ovarian endometriotic deposits adhere to another structure (such as the broad ligament) There is block in the egress of menstrual fluid produced by cyclical endometriosis Hence the fluid collects and causes the ovarian cortex to invaginate	These develop when endometriotic tissue colonizes preexisting inclusion cysts	Occur when endometriosis gains access to a follicle, such as at the time of ovulation

Different pathogenetic types of ovarian endometriotic cysts.. (Scurry J et al 2001³)

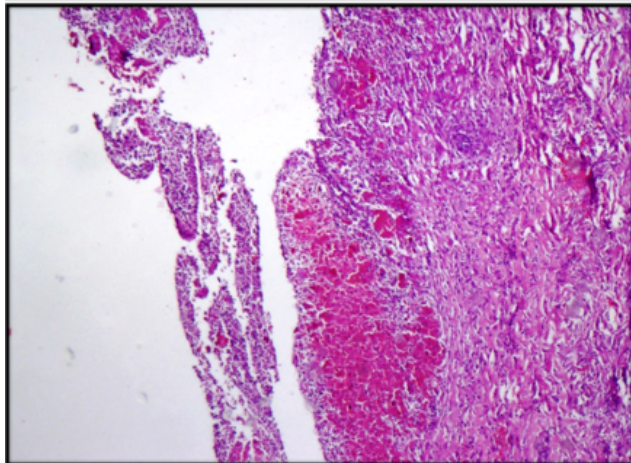


Fig. 1: Endometrial cyst wall with eroded lining epithelium and areas of hemorrhage [H&Ex40]

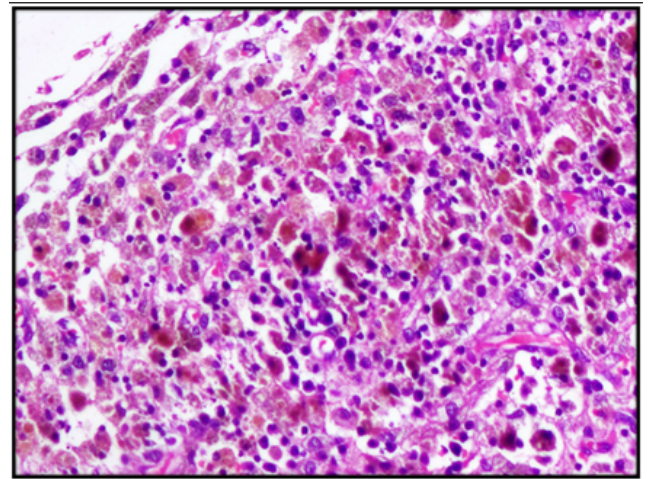


Fig. 3: Cyst wall with hemosiderin laden macrophages [H&Ex200]

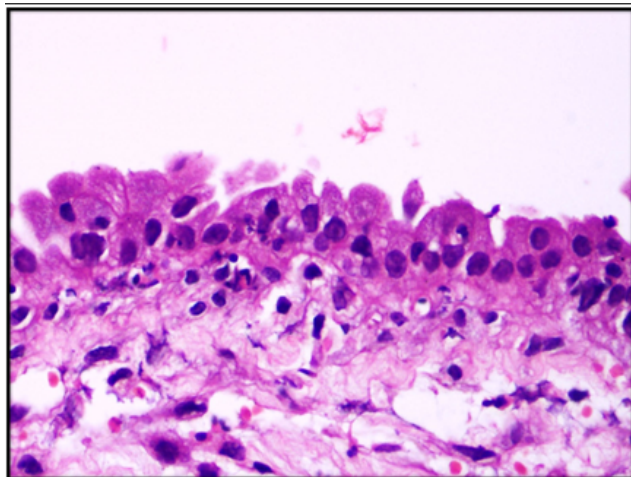


Fig. 2: Cyst wall with the presence of lining epithelium [H&Ex400]

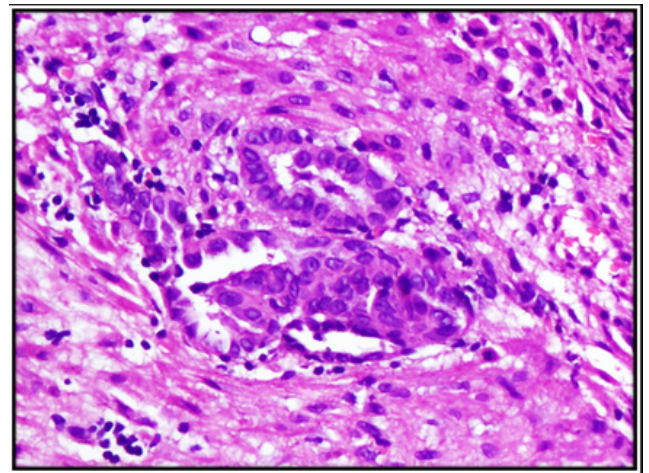


Fig. 4: Cyst wall with endometrial glands [H&Ex200]

pelvic adhesions which can alter ovum release from the ovary. Many studies have demonstrated altered peritoneal function in patients with endometriosis. These patients have often found to have increased peritoneal fluid levels of prostaglandins, tumor necrosis factors and interleukin-1 which in turn can affect the oocyte, sperm, embryo development and function of the fallopian tube. Increase

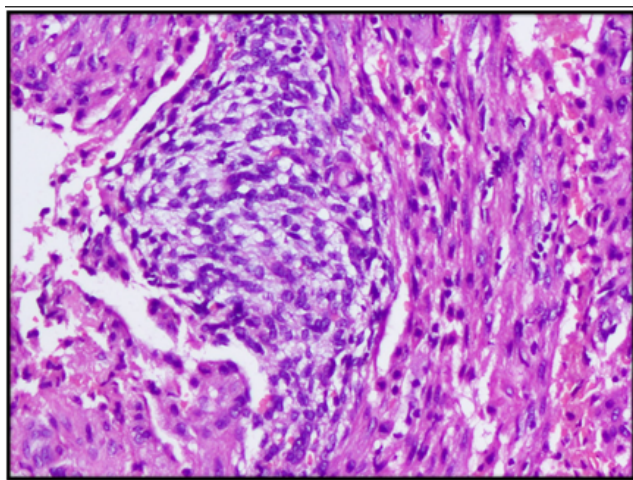


Fig. 5: Cyst wall with endometrial stroma [H&Ex200]

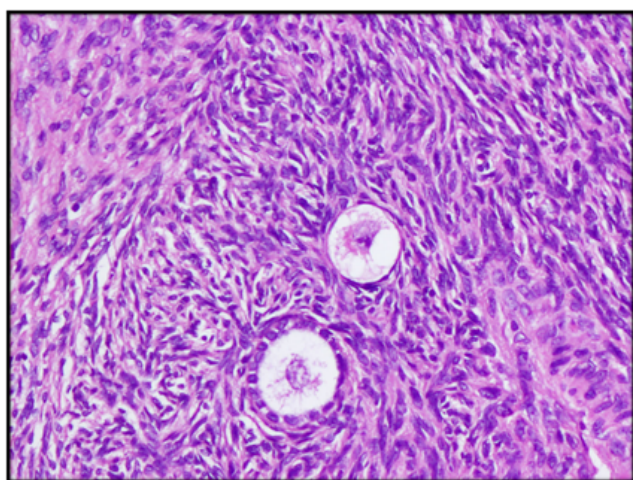


Fig. 6: Adjacent ovarian stroma with primordial follicles [H&Ex200]

Ig A and Ig G antibody levels along with increase in lymphocytes in patients with endometriosis can affect endometrial receptivity and implantation.^{3,6,7}

On gross morphological examination, the size of the lesions in the present study ranged from 4.5 to 18cm and majority of the cases where cystic lesions. Other studies have described endometriosis to appear as “powder burn” or “gunshot” lesions on the ovaries. They may even occur as black, brown-black, or bluish shrunken lesions, nodules, vesicles or tiny cysts containing hemorrhagic material surrounded by grey white areas of fibrosis. A few cystic lesions may be adherent to the peritoneum and adjacent fallopian tubes forming tubo-ovarian masses.^{1,3,10}

On microscopic examination, 68% cases showed cyst wall composed of endometrial lining with a majority of cases showing fibrosis [72.6%] and hemosiderin laden macrophages[80.6%]. Endometrial glands and stroma were present in 53.2% and 61% cases respectively. The diagnosis

of endometriosis on histopathology is often straightforward in those cases where endometrial-type glands and stroma are present. However the diagnosis is often challenging in cases where the endometrial stroma is very scant and when there is extensive fibrosis. The three different types of stroma i.e. fibrous stroma, ovarian stroma, and endometrial stroma may be difficult to distinguish. In such cases multiple serial sections need to be examined. CD10 immunohistochemistry can be of additional value in diagnosing endometriosis in difficult cases where CD10 stains the endometrial stroma.^{4,5,8,11}

Majority of cases in the present study showed the absence of follicles with the presence of primordial follicles in 22% of cases. These findings suggest that the capsule is the invaginated cortex itself and hence their removal affects the ovarian stroma. Thus excision of endometriotic cyst wall may cause loss of functional ovarian tissue. This is of paramount importance in surgical treatment of infertility in patients presenting with endometriosis. Thus ovarian endometriomas could thus affect the response to ovarian stimulation, oocyte recovery, implantation and fertilization rates.^{8,9}

In relation to the treatment aspect, several authors suggest that laproscopic treatment of ovarian endometriotic cysts should consist of drainage & coagulation rather than excision. Controversy still exists regarding the recurrence and pregnancy rates after the two procedures. Few authors suggest that in patients with bilateral endometriosis, fertility preservation with oocyte or ovarian tissue cryopreservation may be considered as a treatment option.^{2,9,11}

5. Conclusion

The present study further emphasizes endometriosis to be an important cause of primary infertility which needs to be recognized and treated appropriately. Recognition of these cysts on histopathological examination can be challenging at times when endometrial stroma is scant and in cases of tubo-ovarian masses where these lesions could mimic malignancy. Excision of endometriotic cyst wall may cause loss of functional ovarian tissue which is extremely important in surgical treatment of infertility in patients presenting with endometriosis. This could in turn affect recovery of oocytes, implantation and fertilization rates.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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