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Histopathological analysis of laparoscopically treated ovarian endometriotic cysts with special reference to loss of follicles

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BACKGROUND: The best operative procedure for the laparoscopic treatment of ovarian endometriotic cysts has yet to be defined. The purpose of this study was to evaluate the association between laparoscopic cystectomy and loss of follicles. METHODS: Videotape records of the laparoscopic removal of 73 ovarian cysts, histologically confirmed in the focal endometrial epithelial lining, were retrospectively reviewed. They were divided into two groups: group 1 (61 cysts) in which the capsule was easily stripped from the underlying ovarian tissue and group 2 (12 cysts) in which the capsule could hardly be stripped from the underlying ovarian tissue. Main outcome measures included attached capsular structures and the number of attached follicles. RESULTS: Microscopically in all group 1 cysts, normal ovarian stroma was attached to the resected side of the capsule. In addition, 30/61 (49.1%) of group 1 cysts were attached to the corpus albicans. The primordial follicle was found within the capsule of 42/61 (68.9%) group 1 cysts. The number of primordial follicles ranged from 1–25 (mean 6.6). In group 2 cysts, no primordial follicles were found. CONCLUSION: The relative ease of removal of the capsules is probably associated with loss of follicles and damage to the ovarian stroma.

Key words: cystectomy/endometriosis/histopathology/laparoscopy/ovary

Introduction

Although endoscopic management of ovarian endometriotic cysts is widely accepted (Dover and Torode, 2000), laparoscopic treatment of ovarian endometriotic cysts remains controversial and the best operative procedure has yet to be defined. A recent prospective randomized study showed that cystectomy resulted in significantly better pain relief and an improved pregnancy rate compared with drainage and coagulation (Berretta *et al.*, 1998). The need for further procedures for ovarian endometrioma after cystectomy was shown to be significantly reduced compared with that after fenestration (Saleh and Tulandi, 1999). However, several authors have recommended drainage and coagulation of the inner lining of ovarian endometriotic cysts rather than cystectomy, because cystectomy has been associated with a higher rate of periadnexal adhesion (Fayez and Vogel, 1991) and loss of cortex (Brosens *et al.*, 1994). Some authors have reported reduced numbers of follicles and oocytes in ovulation induction cycles during IVF in cystectomized patients compared with those in patients who had no previous ovarian surgery (Nargund *et al.*, 1996; Loh *et al.*, 1999).

In the present study, videotape records of the laparoscopic removal of 73 ovarian cysts, histologically confirmed in the endometrial epithelial lining, were reviewed. An association between easy removal of the capsule and loss of follicles was demonstrated.

Materials and methods

Case selection

The first author performed laparoscopic ovarian cystectomies in 69 women with clinically suspected ovarian endometriotic cysts between January 1992 and December 1999. All patients had been referred to the Gynecological Oncology Clinic at Fukuoka University Hospital for treatment of adnexal masses. Videotape records of the laparoscopic removal of 73 endometriotic cysts, histologically confirmed within the focal endometrial epithelial lining, were reviewed. The operating time of the cystectomy procedure, and resecting time for the capsule, were recorded. The size of the cyst, the ease of capsule removal and the extent of adhesion of the cyst to other structures were evaluated.

Laparoscopic procedure

Laparoscopic cystectomy was performed under video control through a subumbilical incision and two lower abdominal incisions using 5 mm scissors and grasping forceps. Abdominal distension was maintained with a laparolift system (Origin Medsystem, CA, USA). All laparoscopic procedures were performed in the abdominal cavity.

Table I. Clinical and histological features of ovarian endometriotic cysts treated with laparascopic cystectomy

	Group 1	Group 2	*P*-value
No. patients	57	12	
No. cysts	61	12	
Age (years)	32.0 ± 5.5	28.4 ± 3.6	0.04
Size (cm)	6.1 ± 1.5	7.3 ± 1.9	0.02
Operating time (min)	96.3 ± 19.2	119.6 ± 26.7	0.001
Resecting time (min)	11.6 ± 5.9	26.3 ± 10.0	< 0.001
Capsule wall thickness (mm)	2.1 ± 0.8	1.8 ± 0.4	NS
No. capsules showing fibrosis	37	4	NS
No. capsules showing follicles	42	0	< 0.001
No. of capsules with corpus albicans attached	30	0	< 0.001

Values are expressed as means ± SD.
NS = not significant.

Figure 1. Laparoscopic removal of a group 1 cyst. The capsule (arrow) was easily stripped from normal ovarian tissue.

The endometriotic cysts were isolated, freed from any adhesions and the contents aspirated. The capsule of the cyst was stripped from the normal ovarian tissue where possible using two atraumatic grasping forceps pulled slowly in opposite directions; additional sharp dissection with scissors was often necessary because the capsule had adhered to the surrounding ovarian tissue in several places. The detached capsule was placed in a bag and removed from the abdominal cavity through subumbilical incision. The remaining ovarian tissue was repaired with a 2–0 dexon continuous suture.

Histological evaluation

Microscopic sections were obtained from the greatest tumour dimension of the cyst. A total of 65 unilateral and four bilateral ovarian cysts were histologically confirmed as ovarian endometriotic cysts because they showed the focal endometrial epithelial lining. Ten unilateral clinically suspected endometriotic cysts were haemorrhagic cysts without epithelial lining. After histological identification, the capsule wall thickness, presence of fibrosis, the number of cysts containing follicles, the number of follicles in a cyst, the depth of penetration of endometrial glands into the wall and the attachment structure of the capsule were histologically evaluated.

Statistical analysis

Statistical analysis was performed using Student's *t*-test (StatView, version 4.57; Abacus Concepts Inc., Berkeley, CA, USA) for patient age, size of the ovarian cyst, thickness of the capsule wall, resecting time and operating time. The χ^2 test was used to assess fibrosis of the cyst, presence of the follicle in the capsule and the attachment of the corpus albicans to the resected side of the capsule. $P < 0.05$ was considered to be statistically significant.

Results

Clinical features

Clinical and histopathological features are summarized in Table I. Patient age ranged from 20–41 years old (mean 31.4). The ovarian cysts measured 4.0–10.5 cm in diameter (mean 6.3). All cysts were found adhered to the broad ligament and/or posterior wall of the uterus. Adhesiolysis was therefore performed in all patients and 64 (87.7%) ovarian endometriotic cysts ruptured during this procedure.

The operating time ranged from 62–178 min (mean 100.2). The resecting time ranged from 5–45 min (mean 15.3) and was <20 min in 58 cases; these capsules were easily stripped from the underlying stroma. The resecting time for 15 cysts was >20 min. Twelve of these 15 capsules could only be stripped with difficulty from underlying ovarian tissue. The other three capsules were easily stripped from the underlying ovarian tissue. The long resecting times were due simply to the large size of the cysts (8.5, 9.0 and 10.5 cm). As a result of these observations, the ovarian endometriotic cysts were divided into two groups: group 1 (61 cysts), in which the capsule was easily stripped from underlying ovarian tissue (Figure 1), and group 2 (12 cysts), in which the capsule was could only be stripped from the underlying ovarian tissue with difficulty. This classification was made blind to histological findings.

The group 2 patients were significantly younger and more had frequently large endometriotic cysts than the group 1 patients. The operating time for group 2 was significantly longer than that of group 1 ($P = 0.001$). The resecting time in group 2 was also significantly longer than that in group 1 ($P < 0.001$).

Microscopic features

The capsule wall thickness in groups 1 and 2 were 2.1 ± 0.8 and 1.8 ± 0.4 mm (mean ± SD) respectively. Attachment of the vascular-rich ovarian stroma to the resected side of the capsule was found in all cases in group 1. Primordial follicles were found in 42 (68.9%) of the group 1 capsules (Figure 2a,b). The number of primordial follicles within each capsule ranged from 1–25 (mean 6.6). Attachment of the corpus albicans to the resected side of the capsule was found in 30 (49.2%) cases in group 1 (Figure 3). Corpus albicans were usually elongated by endometriotic cysts. In contrast, in group 2 no primordial follicles were found in the capsule and neither was the ovarian stroma attached to any capsule (Figure 4). Part of the underlying normal ovarian tissue with follicles was associated with 10 capsules (eight group 1 and two group 2 cysts). Endometrial glands penetrating into the wall were found in nine cysts (eight group 1 and one group 2). The depth from the surface of the deepest penetrating endometrial glands ranged from 1.0–3.0 mm (mean 1.6). Extensive fibrosis of the

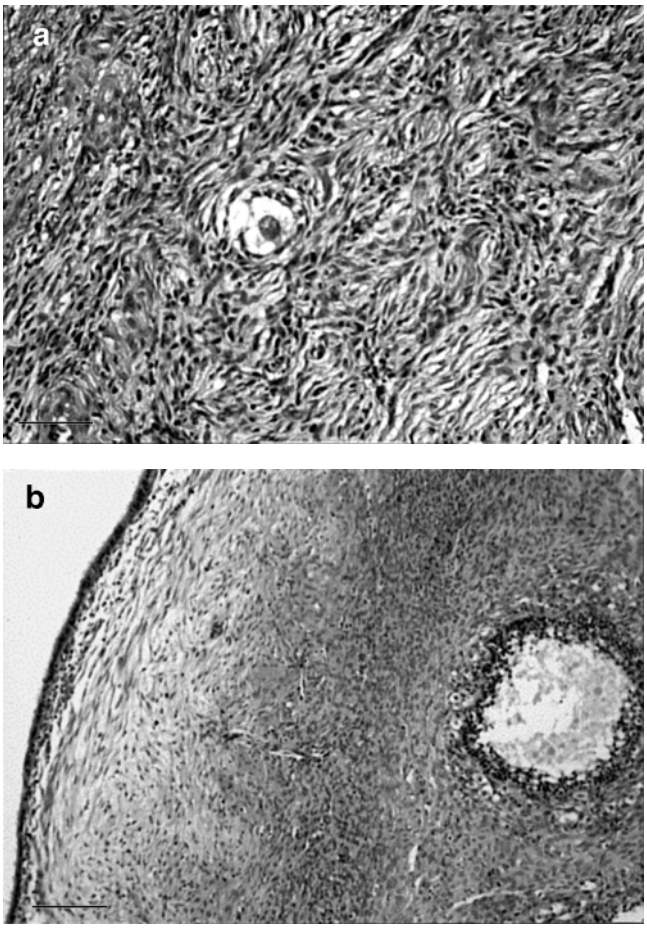

Figure 2. (**a**) A primordial follicle in the wall of a group 1 cyst. (HE. Scale bar = 40 μm). (**b**) A follicle in the wall of a group 1 cyst (scale bar = 100 μm).

Figure 3. The wall of a group 1 cyst. The corpus albicans is attached to the resected side of the cyst wall (scale bar = 200 μm).

Figure 4. The wall of a group 2 cyst. Haemorrhagic debris was seen on the inner aspect of the endometriotic cyst. No ovarian stromal tissue was attached to resected side of the cyst wall (scale bar = 200 μm).

capsule was found in 37 (60.7%) and four (33.3%) cysts in groups 1 and 2 respectively.

Discussion

Hughesdon demonstrated that 93% of ovarian endometriotic cysts are formed by invagination of the cortex after the accumulation of menstrual debris from endometriotic implants (Hughesdon, 1957). In the late stages of cyst formation, the cortex is progressively replaced by pigmentated fibroreactive tissue, changing and masking the original cortex and embedding some of the endometrial tissue and forming a pigmented or dark fibrotic cyst. Microscopic examination of ovarian endoscopy-guided biopsy specimens revealed endometrial tissue in 82% of clinically suspected endometriomas, and occasionally the ovarian cortex with follicles (Brosens *et al.*, 1994). These authors suggested that in most cases the endometrioma is formed by invagination of the cortex. Nisolle and Donnez postulated a different hypothesis for the development of ovarian endometriotic cysts, suggesting that the coelomic metaplasia of invaginated epithelial inclusion is responsible for the pathogenesis of ovarian endometriotic cysts (Nisolle and Donnez, 1997). Although the pathogenesis of ovarian endometriotic cysts is still controversial, two theories support the idea that the endometrial tissue lining is located adjacent to the ovarian cortex. In the present study, 73 (88.0%) of 83 clinically suspected endometriotic cysts showed histologically focal endometrial epithelial lining. All cysts were adherent to the broad ligament and/or the posterior wall of the uterus. The resected capsules of group 1, which were composed histologically of the focal endometrial lining and the fibrotic cortex, often contained primordial follicles. The resected side of the capsule was attached to the vascular-rich ovarian stroma and the elongated corpus albicans. These histological features probably indicate that the resected capsule is the invaginated

cortex itself and ease of removal of the capsule results from damage to the ovarian stroma between the invaginated cortex and the unaffected cortex. Donnez *et al.* suggested that not only is there no real plane of cleavage between the endometrial-type stroma and the ovarian cortex that would facilitate stripping, but also that it is not unusual to find oocytes in the vicinity of the endometrial stroma (Donnez *et al.*, 1996). From the present study, it could be argued that ease of removal of the capsules is associated with loss of follicles and damage to the ovarian stroma. The resected capsules of group 2 did not contain primordial follicles and were not attached to the normal ovarian tissue. The group 2 patients were significantly younger and more frequently had large endometriotic cysts than the group 1 patients. The different features of ovarian endometriotic cysts in groups 1 and 2 may or may not indicate the heterogeneous histogenesis of ovarian endometriotic cysts.

Nezhat *et al.* reported that large endometriomas may develop as a result of the secondary involvement of functional ovarian cysts in the process of endometriosis (Nezhat *et al.*, 1992). The walls of the large cysts were easily removed, but partial removal of the ovarian cortex occurred when resecting the capsule when the wall of the cyst was adhered to underlying ovarian tissue by penetrating endometriosis. Luteal and endometrial linings were found in different areas of large endometriotic cysts. Although serial sections were not done, no ovarian endometriotic cyst showed both luteinized and epithelial lining in the present study. We could not histopathologically demonstrate the secondary involvement of functional ovarian cysts in the process of endometriosis.

Although several authors proposed that the laparoscopic treatment of ovarian endometriotic cysts should consist of drainage and coagulation (Fayez and Vogel, 1991; Brosens *et al.*, 1994) rather than excision, there is controversy over the recurrence and pregnancy rates when comparing the two different laparoscopic procedures (Beretta *et al.*, 1998; Hemmings *et al.*, 1998). In this study, resection of endometriotic cysts was frequently associated with loss of follicles and damage to the ovarian stroma. On this basis, drainage and coagulation treatment for endometriotic ovarian cysts may well be recommended. However, the depth from the surface of the deepest penetrating endometrial glands ranged from 1.0–3.0 mm, whereas the maximum penetration depths for the argon (Keye *et al.*, 1983) and CO_2 (Lasson *et al.*, 1983) lasers used in coagulation procedures have been reported at 0.25 and 0.3 mm respectively. This calls into question whether the complete coagulation of the penetrating endometrial glands can really be achieved under these procedures.

Most laparoscopic surgeons have achieved haemostasis with bipolar electrocautery. No suture was placed in the ovary after ovarian cystectomy (Loh *et al.*, 1999). However, an attempt was made to mimic the laparotomy technique with carefully placed continuous sutures in the remaining ovarian tissue. Laparoscopic suture repair of the ovary is questioned as a means of preventing the periadnexal adhesion (Martin, 1991). There are no data to suggest that suturing is more effective than bipolar electrocautery in preservation of ovarian function. The excessive use of bipolar forceps for haemostasis, especially in hilar areas, may be associated with severe damage to the remaining ovarian stroma.

In the present study, the hard stripping of the capsule from underlying ovarian tissue in group 2 was not associated with a heavy bleeding. Heavy bleeding is usually a major problem when the capsule is resected from an adhesion in hilar areas (Martin, 1991).

In conclusion, the results indicate that the resected capsule is the invaginated cortex itself and ease of removal of the capsule results from damage to the ovarian stroma between the invaginated cortex and the unaffected cortex. The surgical difficulty of group 2 probably depends on excision of the invaginated cortex and not the underlying ovarian stromal tissue. The relative ease of removal of the capsules is also associated with loss of follicles. Although the removal of the capsule has capacity to produce a good outcome (Dover and Torode, 2000), based on this study, a recommendation can be made for drainage and coagulation or a combination of stripping and coagulation when laparosocopic surgeons undertake removal of the capsule to decrease the remaining ovarian tissue.

References

Berretta, P., Franchi, M., Ghezzi, F. *et al.* (1998) Randomized clinical trial of two laparoscopic treatments of endometriomas: cystectomy versus drainage and coagulation. *Fertil. Steril.*, **70**, 1176–1180.

Brosens, I.A., Puttemans, P.J. and Deprest, J. (1994) The endoscopic localization of endometrial implants in the ovarian chocolate cyst. *Fertil. Steril.*, **61**, 1034–1038.

Donnez, J., Nisolle, M., Gillet, N. *et al.* (1996) Large ovarian endometriomas. *Hum. Reprod.*, **11**, 641–646.

Dover, R.W. and Torode, H. (2000) Endometrioma: a review of modern management. *Gynaecol. Endosc.*, **9**, 219–226.

Fayez, J.A. and Vogel, M.F. (1991) Comparison of different treatment methods of endometriomas by laparoscopy. *Obstet. Gynecol.*, **78**, 660–665.

Hemmings, R., Bissonnette, F. and Bouzayen, R. (1998) Results of laparoscopic treatments of ovarian endometriomas: laparoscopic ovarian fenestration and coagulation. *Fertil. Steril.*, **70**, 527–529.

Hughesdon, P.E. (1957) The structure of the endometrial cyst of the ovary. *Br. J. Obstet. Gynaecol.*, **44**, 481–487.

Keye, W.R., Matson, G.A. and Dixon, J. (1983) The use of the argon laser in the treatment of experimental endometriosis. *Fertil. Steril.*, **39**, 26–29.

Lasson, G., Gullberg, B. and Grundsell, H. (1983) A comparison of complications of laser and cold knife conization. *Obstet. Gynecol.*, **62**, 213–217.

Loh, F.H., Tan, A.T., Kumar, J. *et al.* (1999) Ovarian response after laparoscopic ovarian cyctectomy for endometriotic cysts in 132 monitored cycles. *Fertil. Steril.*, **72**, 316–321.

Martin, D.C. (1991) Laparoscopic treatment of ovarian endometriomas. *Clin. Obstet. Gynecol.*, **34**, 452–459.

Nargund, G., Cheng, W.C. and Parsons, J. (1996) The impact of ovarian cystectomy on ovarian response to stimulation during in-vitro fertilization cycles. *Hum. Reprod.*, **11**, 81–83.

Nezhat, F., Nezhat, C., Allan, C. *et al.* (1992) Clinical and histologic classification of endometriomas. Implications for a mechanism of pathogenesis. *J. Reprod. Med.*, **37**, 771–776.

Nisolle, M. and Donnez, J. (1997) Peritoneal endometriosis, ovarian endometriosis, and adenomyotic nodules of the rectovaginal septum are three different entities. *Fertil. Steril.*, **68**, 585–596.

Saleh, A. and Tulandi, T. (1999) Reoperation after laparoscopic treatment of ovarian endometriomas by excision and by fenestration. *Fertil. Steril.*, **72**, 322–324.

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