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Deeply infiltrating endometriosis: pathogenetic implications of the anatomical distribution

Charles Chapron[1,2,5], Nicolas Chopin[1], Bruno Borghese[1], Hervé Foulot[1], Bertrand Dousset[3], Marie Cécile Vacher-Lavenu[4], Marco Vieira[1], Wael Hasan[1] and Alexandre Bricou[1]

[1]Service de Gynécologie Obstérique II, Unité de Chirurgie Gynécologique, [2]Institut Cochin, IFR, [3]Service de Chirurgie Digestive and [4]Sevice Central d'Anatomie et Cytologie Pathologiques, Université Paris V, Assistance Publique – Hôpitaux de Paris (AP-HP), Groupe Hospitalier Universitaire (GHU) Ouest, CHU Cochin, Paris, France

[5]To whom correspondence should be addressed at: Département de Chirurgie Gynécologique, Service de Gynécologie Obstérique II, Clinique Universitaire Baudelocque, 123 Boulevard Port-Royal, CHU Cochin – Saint Vincent de Paul, 75014 Paris, France. E-mail: charles.chapron@cch.ap-hop-paris.fr

BACKGROUND: To investigate whether knowledge of the anatomical distribution of histologically proven deeply infiltrating endometriosis (DIE) lesions contributes to understanding the pathogenesis. METHODS: Observational study between June 1992 and December 2004 (retrospective study between 1992 and 2000; prospective study between 2001 and 2004). Continuous series of 426 patients suffering from pelvic pain who underwent complete surgical exeresis of DIE. DIE lesions were classified according to four different possibilities: (i) Firstly, DIE lesions were classified as located in the anterior or posterior pelvic compartment. (ii) Secondly, DIE were classified as left, median and right. (iii) Thirdly, DIE lesions were classified as pelvic or abdominal. (iv) Fourthly, DIE lesions that could present in a right and/or left location were classified as unilateral or bilateral. RESULTS: These 426 patients presented 759 histologically proven DIE lesions: bladder (48 lesions; 6.3%); uterosacral (USL) (400 lesions; 52.7%); vagina (123 lesions; 16.2%); ureter (16 lesions; 2.1%) and intestine (172, 22.7%). DIE lesions are significantly more often located in the pelvis (n = 730 lesions) than in the abdomen (n = 29 lesions) ($P < 0.0001$). Pelvic DIE lesions are significantly more often located in the posterior compartment of the pelvis [682 DIE lesions (93.4%) versus 48 DIE lesions (6.6%); $P < 0.0001$]. Pelvic DIE lesions are significantly more frequently located on the left side. For patients with unilateral pelvic DIE lesions, the anatomical distribution is significantly different in the three groups: left (172 lesions; 32.0%), median (284 lesions; 52.8%) and right (82 lesions; 15.2%) ($P < 0.0001$). For patients with lateral lesions, left DIE lesions (172 lesions; 67.8%) were found significantly more frequently than right DIE lesions (82 lesions; 32.2%) ($P < 0.0001$). A similar predisposition was observed when we included patients with bilateral pelvic DIE lesions ($P = 0.0031$). The same significantly asymmetric distribution is observed for total (pelvic and abdominal) DIE lesions. CONCLUSIONS: Our results demonstrate that distribution of DIE lesions is asymmetric. It is possible that this is related to the anatomical difference between the left and right hemipelvis and to the flow of peritoneal fluid. These findings support the hypothesis that retrograde menstruation of regurgitated endometrial cells is implicated in the pathogenesis of DIE.

Key words: anatomical distribution/deeply infiltrating endometriosis/implantation/pathogenesis/retrograde menstruation

Introduction

Endometriosis is a very controversial and enigmatic disease (Garry, 2004), and many theories regarding the pathogenesis have been advanced. Two physiopathological hypotheses are the most often proposed to explain the pathogenesis of endometriosis. The first theory is that of retrograde menstruation in which the lesions would be secondary to implantation and proliferation of regurgitated endometrial cells in an ectopic situation (Sampson, 1927). The second theory is that of metaplasia (Meyer, 1919), either of the celomic metaplasia (Gruenwald, 1942) or Mullerian remnants metaplasia (Donnez *et al*., 1995).

There are three types of endometriosis: superficial endometriosis, ovarian endometrioma and deeply infiltrating endometriosis (DIE). DIE is a specific entity (Cornillie *et al*., 1990) histologically defined in arbitrary manner when endometriotic lesions extend more than 5 mm underneath the peritoneum (Koninckx *et al*., 1991). DIE is responsible for painful symptoms (Fauconnier and Chapron, 2005) whose severity is strongly correlated with the depth of the DIE lesions (Koninckx *et al*., 1991; Porpora *et al*., 1999; Chapron *et al*., 2003a).

If retrograde menstruation participates in the physiopathology of endometriosis, it is logical to consider that the anatomical pattern of endometriotic lesions would be determined by

factors (gravidity, proximity to the site of abdominal entry, anatomical considerations, etc.) influencing the distribution and implantation of endometrial cells in the abdominal cavity. Concerning superficial endometriosis, several works have shown that lesions were most often located in the posterior compartment of the pelvis (Dmowski and Radwanska, 1984; Jenkins *et al*., 1986; Ishimaru and Masuzaki, 1991; dell'endometriosi, 1994) and on the left side (Al-Fozan and Tulandi, 2003; Parazzini, 2003). Unlike non-endometriotic benign ovarian cysts (Vercellini *et al*., 2000c), ovarian endometriomas are significantly more frequent on the left ovary (Vercellini *et al*., 1998; Al-Fozan and Tulandi, 2003; Sznurkowski and Emerich, 2005). Recurrent ovarian endometriomas are more frequent on the left ovary (Vercellini *et al*., 2002), and the overall rate of endometriosis recurrence was found to be significantly higher when the left ovary was involved (Ghezzi *et al*., 2001).

Very little work has been devoted to the analysis of the location of DIE lesions. Recently, a surgical DIE classification was proposed based on anatomical distribution of the lesions with a recommended surgical management for each DIE location (Chapron *et al*., 2003b). The sole aim of this publication was to specify the methods of surgical treatment for patients presenting DIE. To our knowledge, only two other authors (Vercellini *et al*., 2000b, 2004; Chapron *et al*., 2001a) have studied the distribution of DIE lesions with the aim of attempting to understand the pathogenesis better. These studies conclude that uterosacral ligament (USL) lesions (Chapron *et al*., 2001a), intestinal lesions (Vercellini *et al*., 2004) and ureteral lesions (Vercellini *et al*., 2000b) are more often observed on the left side.

The goal of our work, which is based on a continuous series with a very large number of patients presenting histologically proven DIE, is to establish whether the study of the anatomical distribution of abdomino-pelvic DIE lesions (USL, vagina, bladder, ureter and intestine) can provide a greater understanding of the pathogenesis.

Materials and methods

Between June 1992 and December 2004, a continuous series of 426 patients suffering from pelvic pain underwent complete surgical management (operative laparoscopy or laparotomy) for DIE. The diagnosis of DIE was histologically proven for each patient. Between June 1992 and December 2000, medical, operative and pathological reports of each patient were re-examined retrospectively in blinded fashion by two authors. Disagreements were resolved by discussion with a third gynaecologist author. The same analysis was performed prospectively for patients operated between January 2001 and December 2004. DIE lesions were classified according to five locations: (i) bladder, when lesions infiltrate the bladder muscularis propria (Chapron and Dubuisson, 1999); (ii) USL, when lesions infiltrate only the USL(s) (Chapron and Dubuisson, 1996); (iii) vaginal, when lesions infiltrate the anterior rectovaginal pouch, posterior vaginal fornix and retroperitoneal area between the anterior rectovaginal pouch and posterior vaginal fornix (Chapron *et al*., 2001b; Martin and Batt, 2001); (iv) ureteral when DIE lesions infiltrate the ureteral wall (intrinsic ureteral endometriosis) or when external ureteral compression by DIE lesions is responsible for a ureteral obstruction (extrinsic ureteral endometriosis) (Clement, 1994) and (v) intestinal, when lesions involve the muscularis propria of the bowel. When a patient presented multiple DIE locations, we classified her in the stage corresponding to the worst one (Chapron *et al*., 2003b). According to the definition, we classified lesions in the following order from least to worst: USL, vagina, bladder, intestine and ureter. We studied the DIE location(s) for each patient according to the above criteria, i.e.: bladder, USL, vagina, ureter and intestine. Concerning the intestinal DIE lesions, the different locations were the following: rectum, recto-sigmoid junction, sigmoid colon, descending colon, transverse colon, ascending colon, appendix, ileocaecum junction, small intestine and omentum. DIE lesions were classified according to four different possibilities. Firstly, DIE lesions were classified as located in the anterior or posterior pelvic compartment. By definition (Jenkins *et al*., 1986), anterior DIE was defined as bladder DIE and posterior DIE included the other pelvic DIE locations: USL, vagina, ureter and intestine. Secondly, DIE were classified as left, median and right. By definition, we classified as left DIE lesions the following: left USL, left ureter, sigmoid colon and descending colon; as median DIE lesions the following: bladder, vagina, rectum, rectosigmoid junction, transverse colon, small intestine and omentum; and as right DIE lesions the following: right USL, right ureter, ascending colon, appendix and ileocaecum junction. Thirdly, DIE lesions were classified as pelvic or abdominal. We classified as abdominal DIE lesions the following: descending colon, transverse colon, ascending colon, appendix, ileocaecum junction, small intestine and omentum. All the other DIE locations (bladder, USL, vagina, ureter, rectum, rectosigmoid junction and sigmoid colon) were considered as pelvic DIE lesions. Fourthly, DIE lesions that could present on either side (right versus left) were classified as unilateral or bilateral.

For each patient, general data were noted (age, parity, gravidity, height, weight and BMI) together with the existence of pelvic pain (dysmenorrhoea, deep dyspareunia and chronic pelvic pain), history of medical and/or surgical treatment for endometriosis, stage of the disease according to the revised American Fertility Society classification (rAFS) (Society, 1985) and mean rAFS scores (total, implants and adhesions) according to the same classification (Society, 1985).

Statistical tests

The proportion of histologically proved DIE lesions was analysed using the χ^2 test. The odds ratio (OR) of the observed frequencies of left- and right-sided lesions were also computed. The 95% confidence interval (95% CI) was computed using the normal approximation. The differences are considered to be statistically significant if $P < 0.05$. All analyses were performed with StatView 5.0 software (SAS Institute Inc.).

Results

Patient characteristics are summarized in Table I. Patient distribution, according to the DIE lesion classification, was as follows: bladder (37 patients; 8.7%); USL (222 patients; 52.1%); vagina (61 patients; 14.3%); ureter (15 patients; 3.5%) and intestine (91 patients; 21.4%) (Table II). These 426 patients presented 759 histologically proven DIE lesions: bladder (48 lesions; 6.3%); USL (400 lesions; 52.7%); vagina (123 lesions; 16.2%); ureter (16 lesions; 2.1%) and intestine (172; 22.7%). Details of intestinal DIE lesions are the following: rectum and rectosigmoid junction (113 lesions; 65.7%); sigmoid colon (30 lesions; 17.4%); caecum and ileocaecal junction (7 lesions; 4.1%); appendix (11 lesions; 6.4%); small bowel (8 lesions; 4.7%) and omentum (3 lesions; 1.7%) (Figure 1). We observed no intestinal DIE lesions on the transverse colon or descending colon. The mean number of DIE lesions per patient was 1.8 ± 1.25 (range 1–7). One hundred and seventy-four patients (n = 174; 40.8%)

Table I. Deeply infiltrating endometriosis (DIE): baseline characteristics

Patients' characteristics (n = 426)	
Age (years)[a]	31.8 ± 5.6 (range 19.3–51.5)
Gravidity[a]	0.5 ± 0.8 (range 0–4)
Parity[a]	0.3 ± 0.6 (range 0–4)
Height (cm)[a]	164.5 ± 6.7 (range 142–194)
Weight (kg)[a]	56.6 ± 8.2 (range 35–96)
BMI (kg/m^2)[a]	20.9 ± 2.9 (range 13.7–33.2)
Previous treatment for endometriosis	
Hormonal treatment (%)	77.7
Surgery (%)	88.9
Mean number of previous surgery	1.1 ± 1.2 (range 0–7)
Preoperative symptoms[b] (%)	
Chronic pelvic pain	87.8
Dysmenorrhoea	79.6
Deep dyspareunia	78.2
Preoperative painful symptoms scores[a,c]	
Dysmenorrhoea	6.8 ± 3.0 (range 0–10)
Deep dyspareunia	4.7 ± 3.5 (range 0–10)
Mean implants score rAFS[a,d]	11.9 ± 11.0 (range 2–46)
Mean adhesions score rAFS[a,d]	20.6 ± 26.8 (range 0–104)
Mean total score rAFS[a,d]	33.1 ± 33.3 (range 2–150)
rAFS Stage[d] (%)	
Stage I	15.5
Stage II	32.6
Stage III	18.3
Stage IV	33.6

[a]Data are presented as mean ± standard deviation.
[b]Sometimes more than one for the same patient.
[c]Visual analogue scale.
[d]Score according to the American Fertility Society Classification (Society, 1985).

Table II. Deeply infiltrating endometriosis (DIE) (n = 426 patients): anatomical location

Main lesion[a]	Number of patients	Associated lesions							
		USL			Va	Bl	Ur	In	Total (%)[b]
		R	L	B					
USL	222	57	109	56					278 (36.6)
Vagina	61	5	6	11	61				94 (12.4)
Bladder	37	2	1	3	3	37			49 (6.5)
Intestine	91	12	12	22	50	8		155	281 (37.0)
Ureter	15	2	4	3	9	3	16	17	57 (7.5)
	426	78	132	95[c]	123	48	16	172	759

B, bilateral; Bl, bladder; In, intestine; L, left; R, right; Ur, ureter; USL, uterosacral ligament; Va, vagina.
[a]According to a previously published surgical classification for deeply infiltrating endometriosis (Chapron *et al*., 2003b).
[b]Number of histologically proven deeply infiltrating endometriosis lesions.
[c]Each lesion of bilateral pair counted as part of pair, so total number of individual lesions = 190.

presented multiple DIE lesions. For patients with multiple DIE lesions (n = 252; 59.2%), the mean number of DIE lesions per patient was 2.9 ± 1.3 (range 2–7).

Among these 426 patients, 18 patients presented abdominal DIE lesions. For one of these 18 patients, the abdominal DIE lesion (appendix) was the only DIE lesion without any associated pelvic DIE lesions. The 17 other patients with abdominal DIE lesions presented associated pelvic DIE lesions. Among the 425 patients with pelvic DIE, 408 (96.0%) patients presented

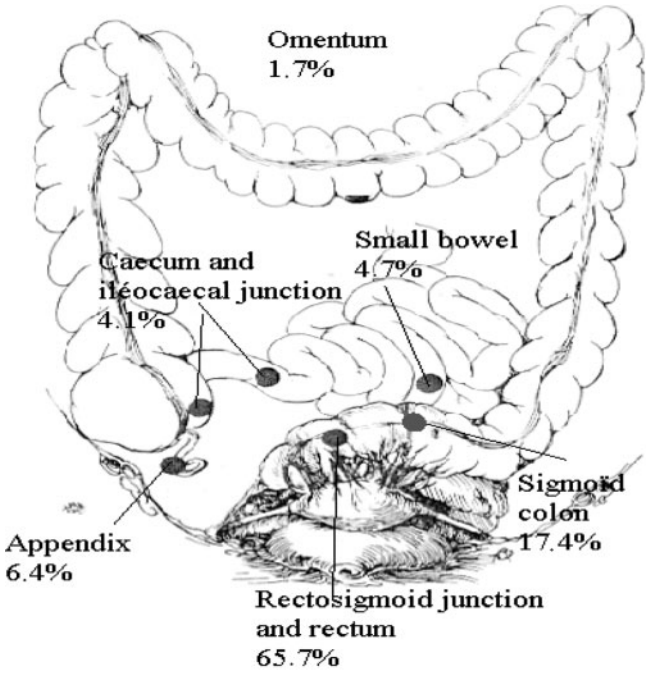

Figure 1. Deeply infiltrating endometriosis of the digestive tract: anatomical distribution.

no associated abdominal DIE lesions. DIE lesions are significantly more often located in the pelvis (n = 730 lesions) than in the abdomen (n = 29 lesions) (P < 0.0001; OR = 25.17; 95% CI = 18.43–34.38).

Pelvic DIE lesions (n = 425 patients; 730 pelvic DIE lesions) are significantly more often located in the posterior compartment of the pelvis [682 DIE lesions (93.4%) versus 48 DIE lesions (6.6%); P < 0.0001; OR = 14.21; 95% CI = 10.71–18.84]. Pelvic DIE lesions are significantly more often found on the left side. For patients with median and unilateral pelvic DIE lesions (n = 330 patients; 538 DIE lesions), the anatomical distribution of these lesions between the three groups differs significantly: left (172 lesions; 32.0%), median (284 lesions; 52.8%) and right (82 lesions; 15.2%) (P < 0.0001). For patients with lateral lesions, left DIE lesions (172 lesions; 67.8%) were found significantly more frequently than right DIE lesions (82 lesions; 32.2%). This is significantly different from the expected proportion of 50% (P < 0.0001; OR = 2.1; 95% CI = 1.47–3.00) (Table III). A similar pattern was observed when we included patients (n = 425) with bilateral pelvic DIE lesions (P = 0.0031; OR = 1.51; 95% CI = 1.16–1.96) (Table III).

Abdominal DIE lesions (n = 29) are more frequently located on the right side (appendix and ileocaecum junction). For patients with abdominal DIE lesions, the anatomical distribution of DIE lesions between the three groups differs significantly: left (0 lesions; 0%); median (11 lesions; 37.9%) and right (18 lesions; 62.1%) (P < 0.0001).

Total (pelvic and abdominal) DIE lesions are significantly more frequently located on the left side. For patients with median and unilateral total DIE lesions (n = 331 patients; 567 DIE lesions), the anatomical distribution of DIE lesions differs significantly between the three groups: left (172 lesions;

Table III. Deeply infiltrating endometriosis (DIE): anatomical distribution of *pelvic* DIE lesions

Main lesions	*n*	Left	Median	Right
Unilateral pelvic DIE lesions (*n* = 330 patients; *n* = 538 DIE lesions)				
USL	210	132	–	78
Vagina	123	–	123	–
Bladder	48	–	48	–
Intestine	143	30	113	0
Ureter	14	10	–	4
Total	538	172[a] (32.0%)	284[a] (52.8%)	82[a] (15.2%)
		172[b] (67.8%)		82[b] (32.2%)
Unilateral and bilateral pelvic DIE lesions (*n* = 425 patients; *n* = 730 DIE lesions)				
USL	400	227	–	173
Vagina	123	–	123	–
Bladder	48	–	48	–
Intestine	143	30	113	0
Ureter	16	11	–	5
Total	730	268[c] (36.7%)	284[c] (39.0%)	178[c] (24.3%)
		268[d] (60.0%)		178[d] (40.0%)

[a]$P < 0.0001$.
[b]$P < 0.0001$.
[c]$P < 0.0001$.
[d]$P = 0.0031$.

Table IV. Deeply infiltrating endometriosis (DIE): Anatomical distribution of *total* DIE lesions

Main lesions	*n*	Left	Median	Right
Unilateral total DIE lesions (*n = 331 patients; n* = 567 DIE lesions)				
USL	210	132	–	78
Vagina	123	–	123	–
Bladder	48	–	48	–
Intestine	172	30	123	19
Ureter	14	10	–	4
Total	567	172[a] (30.3%)	294[a] (51.9%)	101[a] (17.8%)
		172[b] (63.0%)		101[b] (37.0%)
Unilateral and bilateral total DIE lesions (*n* = 426 patients; *n* = 759 DIE lesions)				
USL	400	227	–	173
Vagina	123	–	123	–
Bladder	48	–	48	–
Intestine	172	30	123	19
Ureter	16	11	–	5
Total	759	268[c] (35.3%)	294[c] (38.7%)	197[c] (26.0%)
		268[d] (57.6%)		197[d] (42.4%)

DIE, deeply infiltrating endometriosis.
[a]$P < 0.0001$.
[b]$P = 0.0025$.
[c]$P < 0.0001$.
[d]$P = 0.02$.

30.3%), median (294; 51.9%) and right (101 lesions; 17.8%) ($P < 0.0001$). For patients with lateral lesions, left DIE lesions (172 lesions; 63.0%) were found significantly more frequently than right DIE lesions (101 lesions; 37.0%). This is significantly different from the expected proportion of 50% ($P = 0.0025$; OR = 1.70; 95% CI = 1.21–2.39) (Table IV). A similar pattern was observed when we included patients ($n = 426$) with bilateral total DIE lesions ($P = 0.02$; OR = 1.36; 95% CI = 1.05–1.76) (Table IV).

Discussion

These data suggest that the anatomical distribution of pelvic DIE lesions presents a double asymmetry. Pelvic DIE lesions are more frequently observed in the posterior pelvic compartment and are most often located on the left side. Furthermore, abdominal DIE lesions are far less frequent than pelvic DIE lesions, and unlike these, they are most often located in the right side of the abdominal cavity (appendix and ileocaecum junction).

All these observations plead in favour of the theory of regurgitation and the importance of peritoneal flow patterns in DIE pathogenesis. Other studies have shown that the posterior pelvic compartment is the most frequent site of DIE lesions (Dmowski and Radwanska, 1984; Jenkins *et al*., 1986; Cornillie *et al*., 1990; Ishimaru and Masuzaki, 1991; dell'endometriosi, 1994; Chapron *et al*., 2003b; Redwine, 1999; Bazot *et al*., 2004a). With the patient standing erect, under the effect of gravity, menstrual blood reflux accumulates in the bottom of the Pouch of Douglas, which is the most dependant portion of

the abdomino-pelvic cavity. The effect of gravity also explains why pelvic DIE lesions are more frequently observed than abdominal DIE lesions and why intestinal DIE lesions are preferentially located on the rectum and the recto-sigmoid junction (113 lesions; 65.7% in our experience) (Figure 1). The far lower frequency of deep bladder endometriosis compared with USL, vaginal and rectal DIE can be explained by the anatomy, because the lower limit of the vesico-uterine pouch is located well above the lower limit of the Pouch of Douglas, which lies opposite the middle third of the posterior vaginal wall (Kuhn and Hollyock, 1982; Baessler and Schuessler, 2000). The more the uterus is retroverted, which makes it easier for the peritoneal liquid to flow from the anterior compartment towards the posterior compartment, the more the DIE lesions will be found posteriorly (Jenkins *et al*., 1986).

The anatomical differences between left and right hemipelvis, because of the presence of the sigmoid colon on the left, could explain why pelvic DIE lesions are observed more frequently on the left pelvic side wall. The close anatomical relationship between the sigmoid colon and the left adnexa forms a barrier to pelvic diffusion of menstrual blood reflux, resulting in an anatomical situation that could encourage adhesions and growth of regurgitated endometrial cells on the left pelvic side wall. This anatomical configuration could also explain why endometriomas are more often seen on the left side (Vercellini *et al*., 1998; Al-Fozan and Tulandi, 2003; Parazzini, 2003; Sznurkowski and Emerich, 2005) and why two-thirds of patients with sciatic nerve endometriosis had right-side lesions (Vercellini *et al*., 2003). The sigmoid colon could constitute an obstacle between regurgitated endometrial cells implanted on the left posterolateral pelvic peritoneum and the left lumbosacral plexus, thus protecting the left sciatic nerve (Vercellini *et al*., 2003).

Results of research into the flow of peritoneal fluid support the hypothesis that peritoneal liquid plays a part, together with regurgitated endometrial cells, in DIE pathogenesis. Meyers (1973) demonstrated that intraperitoneal fluid continually follows a circulation through the abdomen. These currents are caused by changes in hydrostatic pressure because of movement of the diaphragm and peristalsis of the bowel. In the erect position, the pressure in the lower abdomen is three times higher than in the upper abdomen (Drye, 1948). The digestive structures and their mesenteric attachments channel the intraperitoneal fluid flow, and variations in intraperitoneal pressure direct this flow clockwise (Foster *et al*., 1981). Four predominant sites have been identified for the preferential, repeated or arrested flow of peritoneal fluid: (i) the pelvic cavity and especially the Pouch of Douglas; (ii) the right lower quadrant at the termination of the small bowel mesentery (caecum and ileocaecum junction); (iii) the superior aspect of the sigmoid mesocolon; and (iv) the right paracolic gutter (Meyers, 1973). Just as for superficial lesions (Jenkins *et al*., 1986) (Table V), the anatomical distribution of DIE lesions correlates with the pathways for the peritoneal fluid flow. A similar observation was made concerning the distribution of intraperitoneal malignant seeding (Meyers, 1973) and acute effusions (Meyers, 1970). Consequently, it cannot be excluded that menstrual regurgitation with deposition and implantation of regurgitated endometrial cells in the abdomino-pelvic cavity could be dependant upon intraperitoneal pressure and the natural flow of fluid in the peritoneal recesses.

Table V. Endometriosis: asymmetric distribution of the lesions

Anterior versus posterior compartment	
Dmowski and Radwanska (1984)	Posterior compartment
Jenkins *et al*. (1986)	Posterior compartment
Cornillie *et al*. (1990)	Posterior compartment
Ishimaru and Masuzaki (1991)	Posterior compartment
dell'endometriosi (1994)	Posterior compartment
Redwine (1999)	Posterior compartment
Chapron *et al*. (2003b)	Posterior compartment
Bazot *et al*. (2004a)	Posterior compartment
Left versus right side	
Superficial endometriosis	
Al-Fozan and Tulandi (2003)	Left side
Jenkins *et al*. (1986)	Left side
Parazzini and Endometriosis (2003)	Left side
Endometriomas	
Vercellini *et al*. (1998)	Left side
Al-Fozan and Tulandi (2003)	Left side
Parazzini and Endometriosis (2003)	Left side
Sznurkowski and Emerich (2005)	Left side
Recurrent endometriosis	
Vercellini *et al*. (2002)	Left side
Ghezzi *et al*. (2001)	Left side
Deeply infiltrating endometriosis	
Uterosacral ligaments	
Chapron *et al*. (2001a)	Left side
Ureter	
Vercellini *et al*. (2000b)	Left side
Intestinal tract	
Vercellini *et al*. (2004)	Left side
All types of pelvic deeply infiltrating endometriosis	
This study	Left side
All types of abdominal deeply infiltrating endometriosis	
This study	Right side
Less common locations	
Sciatic nerve	
Vercellini *et al*. (2003)	Right side
Inguinal endometriosis	
Clausen and Nielsen (1987)	Right side
Candiani *et al*. (1991)	Right side
Kapan *et al*. (2004)	Right side
Diaphragmatic	
Redwine (2002)	Right side
Pleuro-pulmonary	
Foster *et al*. (1981)	Right side
Joseph and Sahn (1996)	Right side
Flieder *et al*. (1998)	Right side
Korum *et al*. (2004)	Right side

These observations would explain the considerably higher frequency of DIE lesions in the pelvis than in the abdomen, together with the fact that these lesions are more often located to the left in the pelvis and the right in the abdomen. This theory helps to explain not only the anatomical distribution of the various types of endometriosis (superficial, endometriomas and DIE) but also that of certain particular endometriotic locations (Table V).

Four other observations plead in favour of regurgitation playing a role for the different types of endometriotic lesions. Firstly, unlike those patients presenting endometriosis without deep lesions, those with DIE have a significantly reduced Douglas pouch depth (Vercellini *et al*., 2000a). This obliteration of the Pouch of Douglas is secondary to the inflammatory

process subsequent to peritoneal implantation of regurgitated endometrial cells, which gives the false impression that deep lesions are of retroperitoneal origin. Magnetic resonance imaging clearly shows that DIE originates from the retrocervical area and not from the rectovaginal septum (Chapron *et al*., 2002). Firstly, the term 'rectovaginal septum endometriosis' is incorrect in the anatomical sense (Chapron *et al*., 2004), as DIE lesions are initially located above the upper border of the rectovaginal septum. Secondly, no peritoneal and/or ovarian endometriotic lesions are seen after tubal ligation (Rock *et al*., 1981), and the rate of endometriosis recurrence at 24 months is significantly less important when endometrial ablation is associated with laparoscopic treatment of endometriosis (Bulletti *et al*., 2001). Thirdly, peritoneal fluid represents a specific microenvironment that could play a role in the pathogenesis of endometriosis (Ramey and Archer, 1993; Koninckx *et al*., 1999). Several studies have shown that ovulation is more frequent on the right side (Potashnik *et al*., 1987; Jarvela *et al*., 2000; Fukuda *et al*., 2001). Greater exposure to progesterone in the right hemipelvis could contribute in this part of the pelvis to set up an inappropriate microenvironment for implantation of endometriotic cells and for developing DIE. Fourthly, the asymmetric nature of pelvic vascularization, because of the entrance of the left ovarian vein into the homolateral renal vein rather than into the vena cava, explains why varicocele occurs more frequently on the left side (Giacchetto *et al*., 1989). This venous stasis on the left side could give rise to local variation in blood stream factors that would affect the development of DIE, which is more dependent on plasma levels than the influence of the peritoneal liquid (Koninckx *et al*., 1999).

In conclusion, our results, together with the vast body of evidence available in the literature, strongly support the implantation theory in DIE pathogenesis and that the role of the peritoneal liquid is essential for understanding the anatomical distribution of DIE lesions.

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