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I.K. ALMOVA¹, E.G. KHILKEVICH¹, V.D. CHUPRYNIN¹,
 A.A. TIKHOMIROVA², A.V. ASATUROVA¹, V.V. CHUR SIN¹

CLINICAL AND DIAGNOSTIC FEATURES OF RETROCERVICAL ENDOMETRIOSIS

¹V.I. Kulakov National Medical Research Center for Obstetrics, Gynecology and Perinatology, Moscow

²N.I. Pirogov Russian National Research Medical University, Moscow

Aim To investigate clinical and diagnostic features of patients with external genital (retrocervical) endometriosis (RCE).

Material and methods The study comprised 44 patients with RCE, who were examined and underwent surgery at the V.I. Kulakov NMRC for OGP from October 2016 to December 2017. Patients were divided into four subgroups. Baseline diagnostic work-up included gynecological and somatic history and diagnostic imaging (transvaginal ultrasound (TVUS), pelvic magnetic resonance imaging (MRI), and colonoscopy). All patients underwent laparoscopic surgery. The type of surgery was chosen based on location, the depth of invasion in the affected organs, the degree of spread in the rectovaginal space, and co-occurrence of colon endometriosis.

Results The main clinical manifestations of RCE included pelvic pain, dysmenorrhea, dyspareunia, infertility, and dyschezia. The absence or presence of the endometriotic infiltration of retrocervical adipose tissue, found during the bimanual and rectovaginal examination, does not rule out infiltrating rectosigmoid endometriosis. Pelvic MRI complements ultrasound clarifying the location and extent of the endometriotic lesion, and involvement of the pelvic organs in the pathological process. Bloating, mucus in stool, dyschezia during menstruation, ultrasound, and MRI findings suggestive of colorectal endometriosis, warrant a colonoscopy. The intraoperative findings complement and refine the data obtained during the pre-operative diagnostic work-up.

Conclusion Patients with RCE need comprehensive diagnostic evaluation with laparoscopy as the final stage, excision of endometriotic lesions, and histological confirmation of the diagnosis.

Keywords: retrocervical endometriosis, pelvic pain, dysmenorrhea, ultrasound, MRI, colonoscopy, laparoscopy.

The authors have no conflicts of interest to report.

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Currently, endometriosis affects about one out of every ten women of reproductive age, or 176 million people worldwide [1]. Endometriosis is associated with infertility in 20-40% of the affected patients and manifests by chronic pelvic pain and/or dysmenorrhea in 70-80% of women.

At this time, the disease remains a challenging issue, and studies investigating its pathogenesis and diagnosis are lacking [2, 3]. In the early stages, endometriosis is practically asymptomatic resulting in late diagnosis in 50% of patients [4].

Important clinical features of external genital endometriosis include pelvic pain, menstrual dysfunction, infertility, and disorders of pelvic organs. The main aspect of diagnosing retrocervical endometriosis (RCE) is a gynecological examination including mandatory rectovaginal examination allowing us to assess the extent of the pathological process, and apply an individual approach to the choice of the diagnostic-therapeutic algorithm [5].

In gynecologic practice the disease is diagnosed using pelvic and abdominal ultrasound, computed and magnetic resonance imaging (MRI), hysteroscopy, laparoscopy, colonoscopy, and cystoscopy [5]. The final diagnosis of endometriosis is based on intraoperative (laparoscopic) visualization of endometriotic lesions and their histological verification [6].

This study aimed to investigate clinical and diagnostic features of patients with external genital (retrocervical) endometriosis.

Material and methods

The study analyzes the results of 44 women of reproductive age with RCE, who were admitted for elective surgery at the Department of General Surgery of the V.I. Kulakov NMRC for Obstetrics, Gynecology and Perinatology of Minzdrav of Russia from October 2016 to December 2017. Written informed consent was obtained from all patients enrolled in the study according to the standards of the Ethics Committee of the Ministry of Health of the Russian Federation. The study was approved by the Ethical Committee of the V.I. Kulakov NMRC for Obstetrics, Gynecology and Perinatology.

The patients underwent clinical and laboratory investigations followed by diagnostic laparoscopy. The patients were divided into four clinical subgroups based on the extent of the pathological process: Ia — patients with external genital (retrocervical) endometriosis without signs of infiltration into adjacent organs (n = 13); Ib — patients with external genital (retrocervical) endometriosis with concurrent endometriotic ovarian cysts (n = 13); Ic — patients with external genital (retrocervical) endo-

metriosis and colon endometriosis ($n = 13$); Id - patients with external genital (retrocervical) endometriosis with concurrent uterine myoma ($n = 5$). Criteria for inclusion in the study: informed consent for participation in the study, histologically verified endometriosis, reproductive age, no hormonal therapy during the last 6 months, the absence of endometrial hyperplasia and malignancy, the absence of acute inflammatory diseases of the pelvic organs, or acute gynecological conditions. All patients underwent general clinical assessment, gynecological examination, rectovaginal examination, and pelvic ultrasound. To detect the location of endometriotic lesions, 24 and 13 patients received pelvic MRI and colonoscopy, respectively. All patients underwent laparoscopic surgery.

Surgical interventions were performed under general endotracheal anesthesia using a standard procedure. The types of surgery in patients with external genital endometriosis included excision of endometriotic lesions within healthy tissues, followed by pathomorphological examination of the surgical specimens.

Mathematical processing included calculations of the arithmetic mean (M), the standard deviation (σ), and the error of the mean (m). The statistical reliability of the obtained data was determined using the parametric Student's test (t -test). For all the results of the studies, the differences were considered reliable at a significance level of 95.0% ($p < 0.05$).

Results

We examined 44 patients aged 18 to 45 (mean 31.5 ± 5.7) years. Endometriosis comorbidities included gastrointestinal diseases, urologic diseases and lower limb varicose veins in 22 (48.9%), 9 (20.4%), and 9 (20.4%) patients, respectively. It should be noted that at the time of surgery these comorbidities were in stable remission and there were no contraindications to the operation.

The previous history of abdominal surgeries is presented in Table. 1. Eight (18.2%), 14 (29.5%), and 7 (15.9%) patients had a history of myomectomy, ovarian cystectomy/resection for ovarian cysts, and diagnostic curettage for suspected endometrial pathology, respectively. Nine (20.5%) patients had a history of appendectomy. All previous surgeries except appendectomy were done by laparoscopic access.

The mean age of menarche was 12.5 ± 1 year. A regular menstrual cycle established within one year. The duration of menstruation was 5.0 ± 1.7 days. Notably, 39 (88.6%) patients had painful menstruations, requiring analgesics for the first two days of the menstrual cycle. Nineteen (43.2%) patients reported heavy menstrual bleeding.

Twenty one women (47.7%) had a history of pregnancy that ended in childbirth, spontaneous miscarriage, and medical abortion in 20 (44.5%), 2 (4.4%), and 8 (17.8%) patients, respectively.

Twenty three (52.3%) women were unable to conceive while having a regular sex life without contraception; 10 them (22.7%) ($p = 0.859$) were from subgroup Ic (RCE with colon endometriosis).

Five (11.4%) ($p > 0.5$), 5 (11.4%) ($p > 0.5$), and 3 (6.8%) ($p = 0.288$) women in subgroup Id (RCE with concurrent uterine myoma), subgroup Ia (RCE), and subgroup Ib (RCE with concurrent endometriotic ovarian cysts), respectively, were infertile. Data on patients' menstrual and reproductive function are presented in Table. 2.

The most common complaint was lower abdomen pain before menstruation deteriorating during menstruation. All patients in subgroup Ia (RCE) and Ib (RCE and endometriotic ovarian cysts) reported pain syndrome. In subgroup Ic (RCE and colon endometriosis), 5 (26%) ($p = 0.302$), 5 (26%) ($p = 0.355$), 3 (23%) ($p > 0.5$), and 8 (18.2%) ($p = 0.238$) patients complained of menstruation related diarrhea with blood in the stools, dyspareu-

Table 1. Previous history of abdominal surgeries

Type of surgery	Number of patients ($n=44$)	
	Absolute number (n)	Percentage (%)
Myomectomy	8	18,2
Cystectomy / resection of the ovary	13	29,5
Hysteroscopy, diagnostic curettage of uterine walls	7	15,9
Appendectomy	9	20,5

Table 2. Characteristics of menstrual and reproductive function

Characteristics of menstrual and reproductive function	Number of patients ($n=44$)	
	Absolute number (n)	Percentage (%)
Cramps before menstruation	5	11,4
Dysmenorrhea	39	88,6
Heavy menstrual bleeding	19	43,2
Moderate menstrual bleeding	25	56,8
Scarce menstrual bleeding	1	2,3
Infertility	23	52,3
Pregnancy	21	47,7
Childbirth	20	44,5
Miscarriage	2	4,4
Abortion	8	17,8

nia, constipation, and intermenstrual rectal bleeding, respectively. In subgroup Id (RCE and uterine myoma), all patients complained of painful menstruation and most of them had heavy menstrual bleeding (4 (80%).

An expert gynecological examination provides valuable diagnostic information. Performed before menstruation, it allows for detection of painful nodular retrocervical infiltrates in accessible pelvic regions. In patients with impaired rectal function and pathological discharge, rectal and rectovaginal examinations revealed painful infiltrates, most often located in the upper part of the rectal ampulla and rectosigmoid colon. It is important to take into account such criteria as the infiltrate size, the mobility of the colonic mucosa above it, its indrawing into the infiltrate tissue, deformity and narrowing of the rectal lumen, the spread of the pathological process to the pararectal tissue and adipose tissue of the lateral pelvic walls, the presence of blood in the rectal lumen. It should be noted that the findings of these examinations allowed only for assuming the presence of colorectal endometriosis, but not to assess the extent of its invasion. In patients with uterine myomas, the bimanual examination showed an enlarged dense uterus with outer contour deformed by myoma nodes, as a rule, partially movable and painful or sensitive when displaced (due to the RCE). Endometriotic cysts were palpated on one or both sides and somewhat posteriorly from the uterus as 3-8 cm gentle elastic formations, sensitive and slightly movable.

Ultrasonography

As a highly sensitive and convenient screening and diagnostic modality in the management of pelvic endometriosis, ultrasonography was performed in all patients, who were examined and underwent surgery at the Department of General Surgery of the V.I. Kulakov NMRC for OGP. Ultrasound examinations were performed using an ALOKA-636 and ALOKA SSD 650 scanners. The abdominal cavity, retroperitoneal space, and pelvic organs were successively scanned by transabdominal, transvaginal, and transrectal ultrasound using 3.5 and 7.5 MHz transducer probes.

RCE was found to have the following characteristic sonographic features: a dense masses in rectovaginal adipose tissue, located both retrocervically and eccentrically in relation to the cervix with local

tenderness; the masses had heterogeneous echotexture, blurred margins, irregular outer contours, and sizes measuring from 1.0 to 2.8 cm.

Ultrasonography can help diagnose not only the simpler forms of endometriosis like endometriotic cysts and uterine myomas but also deep infiltrating genital and extragenital endometriosis including retrocervical masses and endometriosis located in the upper part of the rectal ampulla and rectosigmoid colon (Figures 1 and 2). The photos are courtesy of Professor V.N. Demidov, Senior Researcher at the Department of Ultrasound and Functional Diagnostics of the V.I. Kulakov NMRC for OGP.

Magnetic resonance imaging

MRI is the most accurate non-invasive imaging modality for diagnosing pelvic endometriosis. Detailed visualization of the pathological process and the detection of pelvic anatomical abnormalities caused by deep infiltrating endometriosis provided by MRI enable accurate diagnosis of the disease.

MRI scanning was performed on a Magnetom Harmony MRI scanner (Siemens, Germany). Criteria for assessing the spread of the disease included location, size, and structure of the lesions, the depth of endometriotic invasion in the affected organs, the spread of the endometriotic tissue into the vaginal lumen, the extent of the rectovaginal space infiltration, the depth of invasion into the colorectal wall with the presence or absence of mucosal lesions, the presence of colon endometriosis.

To identify the location of endometriotic lesions, pelvic MRI was performed in 24 patients.

RCE patients had retrouterine endometriotic infiltrates with cervical involvement measuring up to 2.0 cm in diameter. Among 13 patients with colon involvement, endometriosis infiltrated the mucosa, submucosa and muscular layer in 3, 5 and 5 patients, respectively.

The MR images may be represented in different variations mainly as stereoscopic formations infiltrated in the posterior uterine wall, broad ligament of the uterus, uterosacral ligaments, peritoneum of the Douglas' pouch, and fixed to the bowel and the posterior fornix of the vagina (Figure 3). The mass can spread to the bowel wall with or without signs of invasion. MR image of

Fig. 1. Ultrasound image of rectal endometriosis

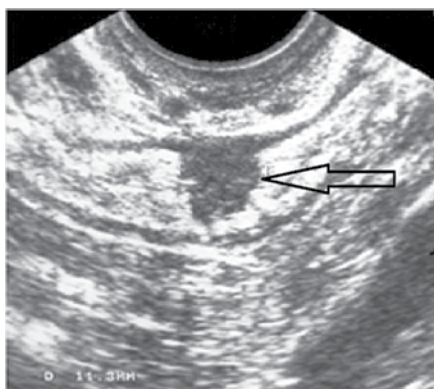


Fig. 2. Ultrasound image of recto-sigmoid endometriosis

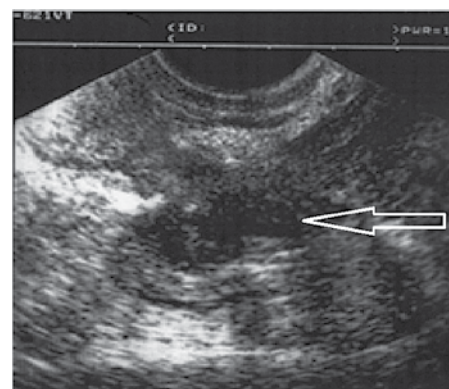
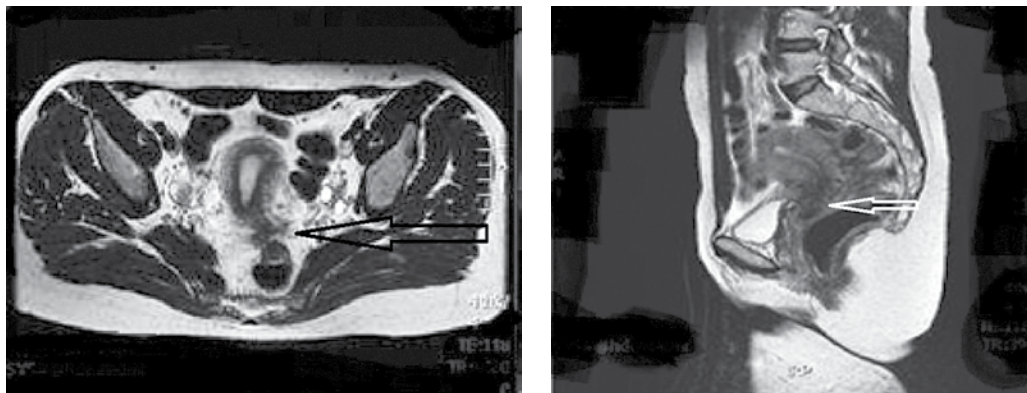


Fig. 3. MR image of RCE



endometriotic ovarian cysts shows a mass in the ovarian stroma with inhomogeneous internal echotexture and cystic and hemorrhagic inclusions.

Pelvic MRI can help diagnose not the consequences of progressive disease, but the involvement of the mucous and muscular layers of the colon wall in the infiltrate and thus allows timely bowel-sparing surgery, avoiding complications such as colon stenosis.

Therefore, we recommend that all patients with deep infiltrating endometriosis undergo pelvic and retroperitoneal MRI before surgery.

Colonoscopy

Among study participants, 13 women with suspected colon endometriosis underwent colonoscopy.

Despite the invasive nature of the procedure, in all cases, it provided valuable information regarding the degree of invasion of endometriosis, which was used in surgical planning to choose the optimal extension of the intervention. Among patients with colon endometriosis ($n = 13$), in 3 (23.1%) 3 (23.1%) 3 (23, 1%), and 4 (30.7%) women endometriotic lesions were located in the upper part of the rectal ampulla, rectosigmoid colon, sigmoid colon, and the lower part of the rectal ampulla, respectively (Fig. 4).

All patients underwent laparoscopic surgery, hysteroscopy, and diagnostic fractional curettage with a sampling of both the endometrial and endocervical mucosa.

Laparoscopy is the gold standard for the diagnosis of endometriosis. For example, the diagnostic accuracy of laparoscopy for ovarian and peritoneal endometriosis is 96% and 100%, respectively. Laparoscopy allows for assessment of the size, number, maturity (by color and shape), and activity of the implants. The disadvantage of the method is the difficulty in determining the depth of infiltrating forms of heterotopia.

At laparoscopy, endometriosis may be visualized as red foci, hemorrhagic vesicles, papular or polypoid lesions; black shrunken foci, classic black foci, white foci, scar tissue with or without pigmentation, atypical foci, other foci, if their presence is confirmed by histological examination. In our study, all patients with RCE, in addition to pelvic peritoneal infiltration had bluish-purple and red endometriotic lesions measuring 0.3-0.5 cm.

Fig. 4. Diagnostic colonoscopy. Infiltrating and stenotic rectal endometriosis invading mucosa



Diagnostic accuracy of laparoscopy for endometriotic cysts is 98-100%. Laparoscopic signs of the endometriotic cyst included cystic ovarian formation sized 3 to 8 cm adhesions with the lateral pelvic wall and/or with the posterior lamina of the broad ligament of the uterus. The lesions had the colors of “burnt gunpowder” or small red or blue spots with the wrinkled surface; they were tar-like, thick, with chocolate-colored contents. Endometriotic lesions were seen on the uterosacral ligaments as whitish nodules, sometimes with a few hemorrhagic inclusions. A clinically important sign of retrouterine endometriosis was the obliteration of the retrouterine space when the rectum is pulled forward to the uterosacral ligaments and to the posterior uterine wall (Figure 5).

The surgical strategy consists in excision of all macroscopically visible endometriotic lesions, resection of the vagina and/or colon if necessary, and restoration of anatomical and topographical continuity of pelvic organs. The extent of surgery was decided based upon the location and depth of endometriotic invasion.

All the patients of the study group underwent excision and coagulation of endometriotic lesions of the pelvic peritoneum. Ovarian resection was performed in all patients of subgroup 1b. Thirteen patients of subgroup 1c underwent colon resection with end-to-end anastomosis; 4 patients treated with colostomy due to a low rectal resection (7-8 cm from the anus).

During the surgery, 5 patients of subgroup 1d underwent myomectomy. Fibroids were primarily subserous-interstitial in location, their size and number ranged from 5 to 7 cm, and from 1 to 3 per patient, respectively.

Endometrium, according to hysteroscopy and histological examination, was found to be in the proliferative phase of the menstrual cycle in 30 (68.1%) and the secretory phase in 14 (31.9%) women. Women with endometrial pathology were excluded from our study.

The final diagnosis of endometriosis is made based on histological findings of either ectopic endometriotic tissue biopsy or surgical specimen (Figure 6).

Discussion

In our study, the main clinical manifestation of infiltrative endometriosis was pelvic pain, dysmenorrhea, dyspareunia, infertility, cyclic hematochezia, dyschezia. According to several authors, in particular, N. Roman [7], endometriosis should be suspected in a woman of reproductive age with pelvic pain and inferti-

tility. Pelvic pain may be either permanent or cyclic. However, these symptoms are not strictly specific for endometriosis, and therefore require differential diagnosis with other diseases. The findings of our study do not contradict the clinical data of the researchers [8].

It should be noted that clinical manifestations of endometriosis depend on the duration of the disease, the depth of the endometriotic invasion and the activity of the process. M. Busard et al. [9], reported that the ectopic endometrium reacts to hormonal stimulation with cyclic bleeding. Clinical manifestations of these processes are diarrhea and/or rectal bleeding during menstruation and/or during the ovulatory "window." These symptoms are considered as a local response resulting from the penetration of the endometrial gland and stroma into the peritoneum, causing smooth muscle proliferation and fibrotic reaction with the formation of dense endometriotic nodules that affect the muscular layer and, ultimately, the colonic mucosa.

Fig. 5. Laparoscopic image of endometriotic infiltrate with colonic involvement

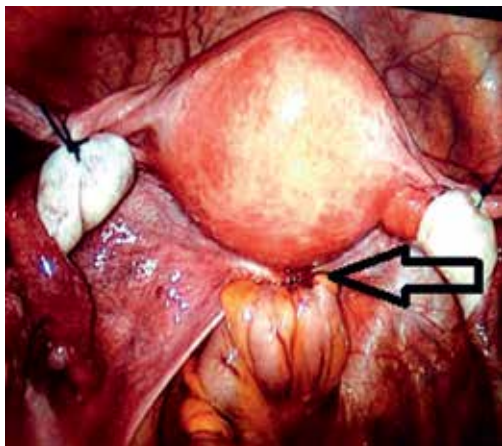
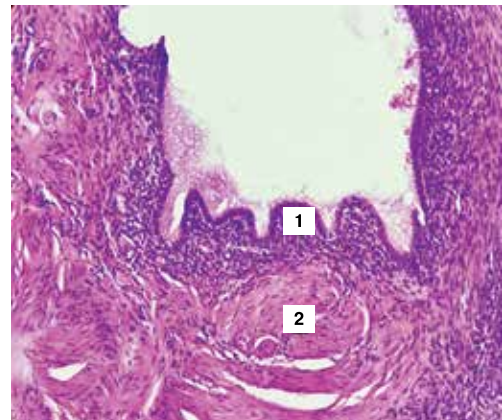
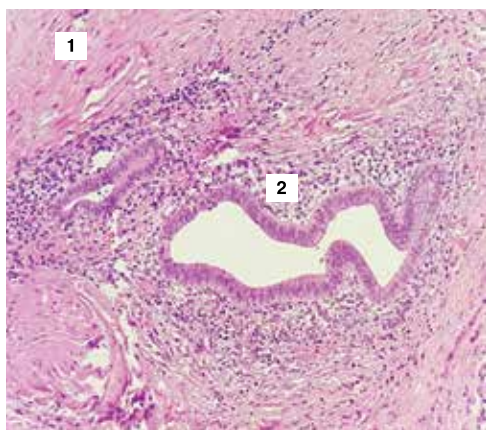


Fig. 6. Endometriosis of the peritoneum



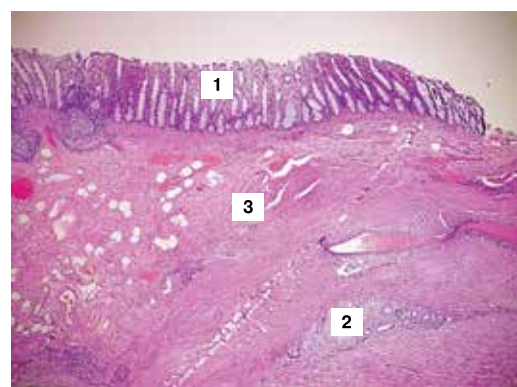
Note: Fragment of fibrous peritoneum with endometriotic heterotopy. Ocular lens is 10x. Objective lens is 20x. Staining with hematoxylin and eosin. 1 - endometrial lining; 2 - fibrous peritoneal tissue.

Fig. 7. Retrocervical endometriosis



Note: Fibrous stroma with endometriotic heterotopy. Ocular lens is 10x. Objective lens is 20x. Staining with hematoxylin and eosin. 1 - retrocervical adipose tissue; 2 - infiltrating endometriotic lesion.

Fig. 8. Colonic wall endometriosis. A fragment of the colonic wall with an infiltrating endometriotic lesion in the muscular layer



Note. Ocular lens is 10x. Objective lens is 4x. Staining with hematoxylin and eosin. 1 - colonic mucosa; 2 - infiltrating endometriotic lesion; 3 - muscular layer of the colonic wall.

Detailed analysis of the patients' history records showed that cyclic hematochezia in combination with pelvic pain syndrome occurs in later stages of infiltrating colorectal endometriosis. This distinguishes endometriosis from colorectal cancer that initially manifests with rectal bleeding. An important feature of rectal bleeding in endometriosis, along with their cyclic character, is its low intensity in the form of blood streaks in the stool, according to our study and the data reported by S. Erdem et al. [10]. It must be remembered that the presence of blood or mucus in the feces requires, first of all, ruling out colorectal cancer.

It should be noted that, that the diagnostic value of the gynecological bimanual and digital rectal examination may vary depending on the location and size of the endometriotic infiltrate. In the course of our work, we found that the absence or presence of an endometriotic infiltrate in retrocervical adipose tissue found by a bimanual and rectovaginal examination does not exclude infiltration of the rectosigmoid colon and additional endometriotic lesions in other parts of the colon. Since the early stages of the disease may be asymptomatic, the endometriotic lesion of the serous or muscular layer of the colon wall is difficult to diagnose, which is confirmed by other researchers [11].

Given the complexity of diagnostic criteria for infiltrative endometriosis based on bimanual and rectal examinations, ultrasound imaging of the expert class and MRI should be used. V.N. Demidov et al. [12] note a rather high sensitivity (95.8%) and specificity (92.6%) of transvaginal echography in the diagnosis of RCE.

The importance of MRI is unquestionable as it provides excellent visualization of the pelvic organs due to the high relative contrast of soft tissues and a complete non-invasiveness. Indications are the widespread endometriosis, especially RCE with the involvement of the colon.

Transvaginal ultrasound and pelvic MRI are mutually complementary diagnostic modalities. The use of one does not exclude the use of another for differential diagnosis and clarification of the location, extent of invasion and involvement of the pelvic organs in the pathological process [13]. Thus, we recommend that all RCE patients have a transvaginal ultrasound and pelvic MRI.

Colonoscopy is used in patients presenting with rectal bleeding with bowel movements to rule out colorectal cancer. Unlike colorectal cancer, which primarily develops from the glandular epithelium of the colonic mucosa, endometriosis affects the colonic wall from the side of the serosa, gradually growing into the colon in the radial direction, or progressively encircling the bowel wall. Colon endometriosis may be located in one or more areas of the colon and primarily requires differential diagnosis with malignant neoplasms. Both types of growth are accompanied by thickening of the colonic wall, formation of the node, deformation, and narrowing of the lumen. With the spread to all layers of the colonic wall, endometriotic lesions appear on the mucosa as undulations, polypoid growths, and in some cases ulceration [14]. Our data are consistent with the results of other researchers that hematochezia occurs in no more than 25% of patients with colonic mucosa invasion [15]. We believe that colonoscopy is indicated in patients with endometriosis if they have bloating,

mucus in the stool, cyclic dyschezia, and/or indirect symptoms of colorectal endometriosis according to ultrasound and, to a greater extent, MRI. Therefore, in our opinion, colonoscopy is necessary for patients with colon endometriosis.

The intraoperative findings complement and refine the data obtained during preoperative diagnostic work-up. Despite direct visualization of the pelvic organs and abdominal cavity, we believe that the above examination should be performed because in patients with deep infiltrating endometriosis we often see the adhesion process involving various pelvic organs without a clear division of the anatomical structures. The findings of ultrasound, MRI, and colonoscopy allow differential diagnosis of the disease, clarify the location of the endometriotic lesions, the degree of involvement of the pelvic organs, determine the optimal extent of surgical intervention, and minimize the risks of injury to organs, nerves and vessels.

Conclusion

Thus, the tendency to affect younger women, complicated and belated diagnosis requires a doctor to perform a more detailed examination even at the stage of collection and analysis of complaints and medical history of patients. The low specificity of most complaints and the lack of attention to the first symptoms of the disease lead to the progression of endometriosis in young women, which negatively affects the reproductive function and quality of their life. None of the above methods of visualization is sufficient to make a diagnosis. A comprehensive examination is necessary with laparoscopy as the final stage, excision of endometriotic lesions, and histological confirmation of the diagnosis.

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Authors' information:

Indira K. Almova, Ph.D. Student at the Department of Surgery, V.I. Kulakov NMRC for OGP of Minzdrav of Russia. Address: 117997, Russia, Moscow, Ac. Oparina str. 4. Tel.: 8 (905) 435-73-17. E-mail: www.gold11@mail.ru
Elena G. Khilkevich, Dr.Med.Sci., Obstetrician-Gynecologist at the Department of Surgery, V.I. Kulakov NMRC for OGP of Minzdrav of Russia. Address: 117997, Russia, Moscow, Ac. Oparina str. 4. Tel.: 8 (495) 438-77-83. E-mail: e_khilkevich@oparina4.ru. ORCID ID: 0000-0001-8826-8439
Vladimir D. Chuprynin, Ph.D., Head of the Department of Surgery, V.I. Kulakov NMRC for OGP of Minzdrav of Russia. Address: 117997, Russia, Moscow, Ac. Oparina str. 4. Tel.: 8 (495) 438-35-75. E-mail: v_chuprynin@oparina4.ru
Aleksandra A. Tikhomirova, 7th Year Student at the Medical Faculty of N.I. Pirogov RNRMU. Tel.: 8 (926) 575-07-89. E-mail: www.gold11@mail.ru
Aleksandra V. Asaturova, Ph.D., Senior Researcher at the Department of Anatomic Pathology, V.I. Kulakov NMRC for OGP of Minzdrav of Russia. Address: 117997, Russia, Moscow, Ac. Oparina str. 4. Tel.: 8 (495) 438-23-11. E-mail: a_asaturova@oparina4.ru
Vyacheslav V. Chursin, Surgeon at the Department of Surgery, V.I. Kulakov NMRC for OGP of Minzdrav of Russia. Address: 117997, Russia, Moscow, Ac. Oparina str. 4. Tel.: 8 (495) 438-78-33. E-mail: v_chursen@oparina4.ru