

CHRONIC PELVIC PAIN AND ENDOMETRIOSIS

Oana-Maria BODEAN*
Diana VOICU¹
Octavian MUNTEANU²
Elvira BRATILA³
Roxana BOHALTEA⁴
Dragos DAVITOIU⁵
Monica CIRSTOIU⁶

ABSTRACT:

CHRONIC PELVIC PAIN IS A SYNDROME WITH A WIDE RANGE OF POSSIBLE CAUSES OF GENITAL AND EXTRAGENITAL ORIGIN. ENDOMETRIOSIS IS A CHRONIC HORMONAL DEPENDENT DISEASE WITH UNSPECIFIC SYMPTOMS, AMONG WHICH CHRONIC PAIN IS PERHAPS THE MOST DISTURBING, MAKING THE PATIENT SEEK FOR MEDICAL ADVICE. TREATMENT OPTIONS ARE VARIED AND MUST BE PROMPTLY APPLIED. THIS ARTICLE HIGHLIGHTS THE MAIN ASPECTS OF CHRONIC PELVIC PAIN AND ENDOMETRIOSIS WITH ELOQUENT EXAMPLES FROM OUR EXPERIENCE.

KEYWORDS: ENDOMETRIOSIS, CHRONIC PELVIC PAIN

INTRODUCTION

Chronic pelvic pain and endometriosis are two of the most disturbing problems that affect an important amount of women and make them search for medical attention. Endometriosis is defined as a chronic disease caused by the presence and effects of endometrial tissue outside the uterus. The ectopic endometrial tissue is a functional one, responding to hormonal changes in the same manner as the one inside the uterine cavity. Endometrial lesions, whether they are small nodules or large cysts develop anywhere in the body. For the physician the greatest challenge is to establish whether chronic pelvic pain is caused by endometriosis or by some other pathology. Pelvic pain related to menstrual cycle, deep dyspareunia,

* PhD Student, MD, Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest, Romania. Correspondence to: oanamb8@gmail.com

¹ MD, Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest

² PhD, Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest

³ MD, Department of Obstetrics and Gynecology, "St. Pantelimon" Hospital Bucharest

⁴ MD, Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest

⁵ MD, Department of General Surgery, University Emergency Hospital Bucharest

⁶ MD, Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest, "Carol Davila" University of Medicine and Pharmacy

gastrointestinal painful symptoms related or unrelated to menstrual cycle, urinary dysfunction, acute abdomen and fertility issues are part of the symptoms and complications induced by endometriosis. Differential diagnosis between endometriosis and other pain-inducing pathologies is sometimes very difficult to perform. There is a series of investigations that can be done, including MRI and laparoscopy, but according to recent literature studies, biopsy is no longer mandatory. The treatment of endometriosis is applied according to the extension and location of lesions, the severity of symptoms, the patient's age and her desire of preserving fertility function.

This article presents a series of characteristic aspects of pelvic pain related to endometriosis and treatment options according to our observations in patients admitted in the Bucharest Emergency Hospital between September 2013 and September 2015.

BACKGROUND

Chronic pelvic pain

Chronic pelvic pain is defined as the presence of non-cyclic pain for at least 6 months localized in the anatomic pelvis and severe enough to cause functional disability that require medical or surgical treatment⁷.

Possible causes of chronic pelvic pain are: gynaecological and obstetric ((post surgical adhesions, pelvic inflammatory disease, endometriosis and adenomyosis), urologic (recurrent or interstitial cystitis, complications of urologic surgery, nephro/urolithiasis), gastrointestinal (irritable bowel disease, chronic inflammatory bowel disease, diverticulosis, polyposis), vascular (pelvic congestion syndrome), musculoskeletal, neurological, psychological. Endometriosis and adhesions are the most frequently responsible for chronic pelvic pain.

Endometriosis

The disease is characterized by the presence and growth of functional endometrial tissue, glands and stroma outside the uterus. The endometrial lesions can be found anywhere in the pelvis and can extend beyond the pelvic organs. The ectopic tissue is influenced by cyclic hormonal changes. There is a wide variety of pain type combinations occurring in women with such disease: dysmenorrhea, dyspareunia, dysuria, non-menstrual chronic pelvic muscle pain, dyschezia.

According to location of foci endometriosis is genital (uterine, tubal, ovarian, intra/extraperitoneal) and extragenital (intestinal, urinary, umbilical, hepatic and pulmonary).

Prevalence of endometriosis in the general population is 0.7-44%. Endometriosis was also found in teenage girls at 1-6 months after menarche and even prior to this event.

According to studies performed by the Association for Endometriosis, 66% of adult women with endometriosis report having symptoms prior to their 20s⁸.

AIM OF STUDY

The aim of this article is to highlight the main characteristics of pelvic pain caused by endometriosis and also to show eloquent examples of patients we treated for endometriosis.

⁷ Rozsnay, Francisc, et al. Outcomes of surgical management of deep infiltrating endometriosis of the ureter and urinary bladder. *JSLs: Journal of the Society of Laparoendoscopic Surgeons*, 2011, 15.4: 439

⁸ Roman, Horace, et al. Surgical management of deep infiltrating endometriosis of the rectum: pleading for a symptom-guided approach. *Human Reproduction*, 2011, 26.2: 274-281; Leyendecker, G.; Wildt, L.; Mall, G. The pathophysiology of endometriosis and adenomyosis: tissue injury and repair. *Archives of gynecology and obstetrics*, 2009, 280.4: 529-538.

CASE EXAMPLES

Case 1. Deep infiltrative endometriosis (EN) diagnosed during cesarian section delivery in pregnant patient. Figure 1 shows endometriosis tumor with large base of implantation, infiltrating the serous coat of the urinary bladder. Figure 2 shows tumor infiltrating vesicouterine peritoneum. Symptoms prior to pregnancy: chronic pelvic pain unresponsive to NSAIDs, constipation, cyclic and non-cyclic back pain, dysmenorhea and dyspareunia. Patient received surgical and hormonal treatment with good outcomes.

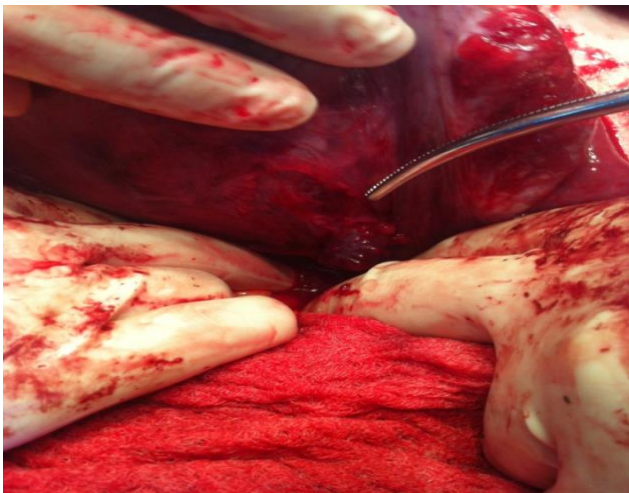


Fig. 1 EN infiltrating urinary bladder.



Fig. 2 EN in the vesicouterine peritoneum

Case 2. Endometriosis cyst and adenomyosis (Fig. 3, Fig. 4) in 34 year-old patient with chronic pelvic pain with progressive dysmenorrhea unresponsive to NSAIDs. The patient is currently under hormonal treatment.



Figure 3- Endometriosis cyst



Figure 4- Adenomyosis

Case 3. Endometriosis nodule (Figure 5) located on the urinary bladder extracted from a patient with progressive dyspareunia, chronic pelvic pain and cystitis unresponsive to medical treatment.



Fig. 5- Vesical endometriosis nodule

DISCUSSIONS

There are a few well-known theories about the physiopathology of endometriosis, but none of them can fully explain the whole process involved⁹:

1. The retrograde menstruation and implantation theory stands that endometrial tissue shed during menstruation is transported via the fallopian tubes into the peritoneal cavity where it implants on the surface of pelvic organs. This theory, however, cannot explain the occurrence of endometriosis in women with Mullerian agenesis or aplasia or in those who did not reach menarche prior to having been diagnosed with endometriosis.
2. The coelomic metaplasia theory holds that endometriosis results from spontaneous transformation (metaplasia) of mesothelial cells derived from the coelomic epithelium located in the peritoneum and pleura. This theory could explain endometriosis in male patients.
3. Vascular or lymphatic dissemination theory could explain extragenital endometriosis.
4. Hormonal theory- development of disease depends on the presence of steroid hormones.
5. Induction theory suggests that the transformation of undifferentiated peritoneal cells into endometrial cells is induced by an endogenous biochemical factor.

The main symptoms of patients with endometriosis are: chronic pelvic pain, back pain, progressive dysmenorrhea, dyspareunia, gastrointestinal disorders, urinary disorders, infertility, acute abdomen (due to rupture of endometriomas), heavy menstrual blood flow, early onset of menstrual cycle.

The mechanism responsible for the pain associated to endometriosis is very complex. It seems to involve the production of growth factors and cytokines by the activated

⁹ Surrey, Eric S., et al. Prolonged GnRH agonist and add-back therapy for symptomatic endometriosis: long-term follow-up. *Obstetrics & Gynecology*, 2002, 99.5, Part 1: 709-719; Leyendecker, G., et al. Endometriosis: a dysfunction and disease of the archimetra. *Human Reproduction Update*, 1998, 4.5: 752-762.

lymphocytes in the endometrial implants. There is also the effect of blood content in the implants and also a direct stimulation of pelvic nerves by compression or infiltration¹⁰.

The nervous pathways⁸ of pain impulses transmission to pelvic organs are illustrated in the table 1:

Spinal segment	Nerves	Organs
T9-T10	Thoracolumbar splanchnic nerves, renal and aortic plexus, ovarian blood vessels via celiac and mesenteric ganglia	Ovaries
T9-T10	Thoracolumbar splanchnic nerves via mesenteric plexus	Upper part of the ureter External 2/3 of fallopian tubes
T11-T12, L1	Thoracolumbar splanchnic nerves via uterine and inferior hypogastric plexes	Fundus uterii, fallopian tubes, broad ligaments, urinary bladder, colon, appendix
S2-S4	Pelvic nerves via pelvic plex	Upper part of Vagina, cervix, uterine isthmus, urethra, uterosacral ligaments
S2-S4	Pudendal nerve, ilioinguinal nerve, genitofemoral nerve, cutaneous posterior femoral nerve	Perineum, vulva

Table 1- The nervous pathways of pain impulses transmission to pelvic organs¹¹

Therefore, parietal endometriosis causes pain in the territory related to the iliohypogastric and ilioinguinal nerves. (T12-L1); ovarian endometriosis may cause pain in the innervation territory of the aortic plexus (T9-T10); an endometrioma can compress the obturator nerve and cause pain in the back of the hip; invasion of different ovarian or uterine ligaments creates pain in the T9-T10, L1-L2 territories. Other locations, such as deep infiltrative endometriosis, ureteral or bladder endometriosis show pain and symptoms related to these areas.

The diagnosis of endometriosis implies 6 major steps: clinical examination, pelvic ultrasound or abdominal ultrasound, CT-scan, MRI, serum markers (CA 125, CA 19-9, PP14, IL-6, TNF- α), laparoscopy¹².

¹⁰ Donnez, J., et al. Laparoscopic excision of rectovaginal tumors. *Atlas of operative laparoscopy and hysteroscopy*, 2007, 63; Harada, T., et al. Apoptosis in human endometrium and endometriosis. *Human Reproduction Update*, 2004, 10.1: 29-38; Fauconier, A.; Chapron, C. Endometriosis and pelvic pain: epidemiological evidence of the relationship and implications. *Human reproduction update*, 2005, 11.6: 595-606.

¹¹ Fauconier, A.; Chapron, C. Endometriosis and pelvic pain: epidemiological evidence of the relationship and implications. *Human reproduction update*, 2005, 11.6: 595-606.

¹² Mol, Ben WJ, et al. The performance of CA-125 measurement in the detection of endometriosis: a meta-analysis. *Fertility and sterility*, 1998, 70.6: 1101-1108; Hornstein, M. D., et al. Prospective randomized double-blind trial of 3 versus 6 months of nafarelin therapy for endometriosis associated pelvic pain. *Fertility and sterility*, 1995, 63.5: 955-962; Speroff, Leon; Fritz, Marc A. (ed.). *Clinical gynecologic endocrinology and infertility*. Lippincott Williams & Wilkins, 2005.

Clinical examination provides information about pelvic organs suggesting endometriosis. Such clinical findings are: sensitivity and nodules of the uterosacral ligaments (active lesions or scars); ovarian cystic mass adherent to pelvic organs or mobile masses (ovarian endometriosis); retroverted, relatively fixed uterus. Examining the patient during the menstrual period increases the chances of diagnosing endometrial nodules and evaluating pain level. Clinical pelvic examination also excludes other pathologies that may require immediate medical or surgical care.

Differential diagnosis of pelvic pain includes pain of different origin, such as: uterine (primary dysmenorrhea, adenomyosis), intestinal (irritable bowel disease, chronic constipation), urinary (cystitis, urinary infection, renal colic), ovarian (pain during ovulation, complicated ovarian cysts), adnexal (haematosalpinx, ectopic pregnancy, pelvic inflammatory disease)¹³.

Transvaginal ultrasound allows the identification of ovarian masses and of other possible causes of pelvic pain but does not reveal peritoneal lesions or adhesions.

CT-scan is used to diagnose extragenital endometriosis and to evaluate the extension of the disease. MRI can help identifying small endometrial nodules, endometrial plaques and larger endometriomas.

Serum biomarkers are also used to evaluate endometriosis, but there is no specific marker for this disease. CA-125 is found in the epithelium of fallopian tubes, endometrium, endocervix, pleura and peritoneum. It is a biomarker for ovarian cancer but although it may have elevated levels in patients with endometriosis, it has low sensitivity and therefore it cannot be used as a screening test for endometriosis. An elevated level of CA-125 is correlated to the severity of endometriosis¹⁴. CA 19-9 is a serum biomarker specific to cancer of the pancreas but an elevated level does correlate to the severity of endometriosis¹⁵. Other biomarkers such as IL-6 or TNF-alpha are used in different studies but are not specific.

Laparoscopy is the main investigation used to diagnose endometriosis. A systematic examination of the pelvic and abdominal cavities reveals typical and atypical lesions. Typical lesions are reddish, “powder-burn”- like or “gunshot”-like lesions or larger endometriomas. Atypical lesions are white, clear, vesicular or haemorrhagic. Colors vary from red, white, yellowish to dark black lesions of different morphology: vesicles on the peritoneal surface, holes in the peritoneum, stellar lesions right on the peritoneal or organ surface or deep infiltrative endometriosis. The extension of lesions in teenage patients do not correlate to the severity of disease, most adolescent girls being diagnosed in stage I or II¹⁶.

Recent guides do not consider biopsy and histopathology to be mandatory. Histopathological examination finds ectopic endometrial stroma and glands. Hemosiderine deposits and fibro-muscular metaplasia are often found.

The classification of endometriosis (E) according to the American Society of Reproductive Medicine¹⁷ is shown in table 2.

¹³ Cirstoiu, M., et al. Case study of a rare form of endometriosis. *Journal of medicine and life*, 2013, 6.1: 68; Cirstoiu M, Secara D, Bodean O, Munteanu O-Endometriosis in adolescents – *The 8th Congres ofl Romanian Society of Endocrinologic Gynecology* 12-14 June 2014, Bucharest, Romania

¹⁴ Harel, Zeev- Dysmenorrhea in adolescents and young adults: etiology and management. *Journal of Pediatric and Adolescent Gynecology*, 2006, 19.6: 363-371; Laufer, M. R. Premenarcheal endometriosis without an associated obstructive anomaly: Presentation, diagnosis, and treatment. *Fertility and Sterility*, 2000, 74.3: S15.

¹⁵ Fedele, Luigi, et al. Stage and localization of pelvic endometriosis and pain. *Fertility and sterility*, 1990, 53.1: 155-158.

¹⁶ Vernon, M. W., et al. Classification of endometriotic implants by morphologic appearance and capacity to synthesize prostaglandin F. *Fertility and sterility*, 1986, 46.5: 801-806

¹⁷ American Society for Reproductive Medicine revised classification of endometriosis, 1985. (American Fertility Society: Revised American Fertility Society Classification for Endometriosis. *Fertility Sterility* 43:351,1986)

<p>Stage I (minimum) total 4p peritoneum: superficial E 1-3 cm 2p right ovary: superficial E<1cm 1p hidden adhesions 1/3 1p</p> <p>Stage II (light) total 9p peritoneum: profound E>3cm 6p right ovary : superficiala E<1cm 1p hidden adhesions< 1/3 1p left ovay: superficial E<1cm 1p</p> <p>Stage III (moderate) total 26p peritoneum: profound E >3cm 6p cul de sac: partially obliterated 4p left ovary: profound E 1-3cm 16p</p> <p>Stage III (moderate) total 30p peritoneum: superficial E> 3cm 4p right fallopian tube: hidden adhesions <1/3 1p right ovary: hidden adhesions<1/3 1p left fallopian tubes: profound adhesions<1/3 16p left ovary: profound E 1-3cm 4p dense adhesions<1/3 4p</p>	<p>Stage IV (severe) total 114p peritoneum : profund E>3cm 6p cul de sac: complete obliteration 40p right ovary: profound E 1-3cm 16 p dense adhesions<1/3 4p left fallopian tube: dense adhesions>2/3 16p left ovary: profound E 1-3cm 16p dense adhesions>2/3 16p</p> <p>Stage IV (severe) total 52p peritoneum: superficial E>3cm 4p left ovary: profound E<1cm 32p profound adhesions<1/3 8p left fallopian tube: dense adhesions<1/3 8 p</p>
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Table 2- Classification of endometriosis (American Society of Reproductive Medicine)¹⁸

Treatment of endometriosis depends on the severity of symptoms, of lesion extension, patient's age and her desire for preserving fertility function. Treatment options include¹⁹:

A. Expectative

B. Medical treatment

a) NSAIDs

b) Hormonal treatment: Combined oral contraceptive pills, progestative pills, androgens, GnRH analogues, aromatase inhibitors.

C. Surgical treatment: conservative or radical

Expectative can be chosen in asymptomatic patients or in those with mild symptoms. Studies show that these patients will eventually have a lower fertility rate than those surgically managed.

Medical treatment using NSAIDs as first line to alleviate dysmenorrhea and chronic pelvic pain is successful in patients with minimum or mild endometriosis. The drugs inhibit COX-1 and COX-2, which are the enzymes responsible for prostglandine synthesis, inflammation and pain. COCs inhibit gonadotropin secretion, diminish menstrual blood flow and implant decidualization. Therefore they reduce dysmenorrhea but do not reduce dyspareunia and non-cyclic pain²⁰.

Progestatives reduce estrogen effects on the endometrium, causing atrophy. Side effects are: acne, edema, weight gain, irregular menstrual bleeding, depression, breast congestion, low

¹⁸ American Society for Reproductive Medicine revised classification of endometriosis, 1985. (American Fertility Society: Revised American Fertility Society Classification for Endometriosis. *Fertility Sterility* 43:351,1986)

¹⁹ Meigs, Joe Vincent. Endometriosis—its significance. *Annals of surgery*, 1941, 114.5: 866.

²⁰ Meigs, Joe Vincent. Endometriosis—its significance. *Annals of surgery*, 1941, 114.5: 866; Witz, Craig A.; Burns, William N. Endometriosis and infertility: is there a cause and effect relationship? *Gynecologic and obstetric investigation*, 2002, 53.Suppl. 1: 2-11.

bone density. Treatment options are: Medroxyprogesterone acetate, Levonorgestrel-releasing IUDs, selective progesterone receptor modulators (SPRMs).

Androgens directly inhibit the growth rate of endometrial implants, but have severe and teratogenic side effects and are rarely used. GnRh analogues reduce COX-2 levels and also reduce implant size and pain level but require “add-back therapy” to diminish side effects and are rarely used in adolescents. Aromatase inhibitors inhibit estrogen production in the ovaries and in the endometrial implants, but have severe side effects in reducing bone mass, similar to GnRH analogues.

Surgical treatment uses laparoscopy or laparotomy, the two techniques having same efficacy. Surgery releases pain in 63% of patients, as according to literature studies, but in adolescents conservative surgery must be followed by medical treatment to reduce recurrence.

CONCLUSIONS

We conclude this article stating that the majority of patients who do not respond to conventional treatment against chronic pelvic pain usually have endometriosis. The unspecific symptoms of pelvic endometriosis make it difficult for the clinician to deliver an early diagnosis.

As in the cases shown above, in which we performed surgical treatment followed by medical treatment, we consider that an adequate and prompt management is necessary to reduce disease progression and consequences and to improve the quality of life of patients dealing with chronic pelvic pain and endometriosis.

REFERENCES

1. **Rozsnay, Francisc**, et al. Outcomes of surgical management of deep infiltrating endometriosis of the ureter and urinary bladder. *JSLs: Journal of the Society of Laparoendoscopic Surgeons*, 2011, 15.4: 439
2. **Roman, Horace**, et al. Surgical management of deep infiltrating endometriosis of the rectum: pleading for a symptom-guided approach. *Human Reproduction*, 2011, 26.2: 274-281.
3. **Leyendecker, G.; Wildt, L.; Mall, G.** The pathophysiology of endometriosis and adenomyosis: tissue injury and repair. *Archives of gynecology and obstetrics*, 2009, 280.4: 529-538.
4. Surrey, Eric S., et al. **Prolonged GnRH agonist and add-back therapy for symptomatic endometriosis: long-term follow-up.** *Obstetrics & Gynecology*, 2002, 99.5, Part 1: 709-719.
5. Leyendecker, G., et al. **Endometriosis: a dysfunction and disease of the archimetra.** *Human Reproduction Update*, 1998, 4.5: 752-762.
6. Donnez, J., et al. **Laparoscopic excision of rectovaginal tumors.** *Atlas of operative laparoscopy and hysteroscopy*, 2007, 63.
7. Harada, T, et al. **Apoptosis in human endometrium and endometriosis.** *Human Reproduction Update*, 2004, 10.1: 29-38.
8. Fauconier, A.; Chapron, C. **Endometriosis and pelvic pain: epidemiological evidence of the relationship and implications.** *Human reproduction update*, 2005, 11.6: 595-606.
9. Mol, Ben WJ, et al. **The performance of CA-125 measurement in the detection of endometriosis: a meta-analysis.** *Fertility and sterility*, 1998, 70.6: 1101-1108.
10. Hornstein, M. D., et al. **Prospective randomized double-blind trial of 3 versus 6 months of nafarelin therapy for endometriosis associated pelvic pain.** *Fertility and sterility*, 1995, 63.5: 955-962.
11. **Speroff, Leon; Fritz, Marc A.** (ed.). Clinical gynecologic endocrinology and infertility. *Lippincott Williams & Wilkins*, 2005.
12. **Cirstoiu, M.**, et al. Case study of a rare form of endometriosis. *Journal of medicine and life*, 2013, 6.1: 68.
13. **Cirstoiu M, Secara D, Bodean O, Munteanu O**-Endometriosis in adolescents – *The 8th Congres ofl Romanian Society of Endocrinologic Gynecology* 12-14 June 2014, Bucharest, Romania
14. **Harel, Zeev**- Dysmenorrhea in adolescents and young adults: etiology and management. *Journal of Pediatric and Adolescent Gynecology*, 2006, 19.6: 363-371.
15. **Laufer, M. R.** Premenarcheal endometriosis without an associated obstructive anomaly: Presentation, diagnosis, and treatment. *Fertility and Sterility*, 2000, 74.3: S15.
16. **Fedele, Luigi**, et al. Stage and localization of pelvic endometriosis and pain. *Fertility and sterility*, 1990, 53.1: 155-158.
17. **Vernon, M. W.**, et al. Classification of endometriotic implants by morphologic appearance and capacity to synthesize prostaglandin F. *Fertility and sterility*, 1986, 46.5: 801-806.
18. American Society for Reproductive Medicine revised classification of endometriosis, 1985. (American Fertility Society: Revised American Fertility Society Classification for Endometriosis. *Fertility Sterility* 43:351,1986)
19. **Meigs, Joe Vincent.** Endometriosis—its significance. *Annals of surgery*, 1941, 114.5: 866.
20. **Witz, Craig A.; Burns, William N.** Endometriosis and infertility: is there a cause and effect relationship? *Gynecologic and obstetric investigation*, 2002, 53.Suppl. 1: 2-11.