Journal of Surgical Sciences (2015) Vol. 19 (1) : 25-30

JOURNAL OF SURGICAL SCIENCES

Review Article

EXTERNAL ENDOMETRIOSIS

Nazneen Kabir[1], Dilruba Akhter[2], Hashrat Jahan[3]

Endometriosis is a fairly common and puzzling disease affecting women in their reproductive years. It is still poorly understood despite a high and still increasing publication rate of over 500 articles a year i.e 455, 426, 448, 504 and 534 in the last 5 years respectively[1]. Endometriosis is a hormonal and immune system disease in which cells similar to that which line the uterus (endometrium) grow outside the uterine cavity, most commonly, the peritoneum. Endometriosis is either genital (within the genital organs, uterus and ovaries) and extragenital (outside the reproductive system: the navel, intestines etc)[2]. Genital endometriosis, is in turn divided into external and internal. External genital endometriosis tissue, similar to the endometrium, is located outside the uterine cavity on the organs and pelvic peritoneum forming nodules, tumors, lesions, implants or growths[3]. Endometriotic implants contain estrogen, progesterone, and androgen receptors[4]. These growths induce a chronic inflammatory reaction and can cause pain, infertility, and other problems. The most common locations of endometrial growths are in the abdomen involving the ovaries, fallopian tubes, the ligaments supporting the uterus, the area between the vagina and the rectum, the outer surface of the uterus, and the lining of the pelvic cavity. Sometimes the growths are also found in abdominal operation scars, on the intestines or in the rectum, on the bladder, vagina, cervix, and vulva. In endometriosis, displaced endometrial tissue continues to act as it normally would-it thickens, breaks down and bleeds with each menstrual cycle. Because this displaced tissue has no way to exit the body, it becomes trapped. When endometriosis involves the ovaries, cysts called endometriomas may form. Surrounding tissues can become irritated, eventually developing scar tissue and adhesions.

Endometriosis can cause pain, sometimes severe especially during the menstrual period. Fertility problems also may develop. It is considered to be one of the most important causes of pelvic pain and of infertility. The pain is the most common cause of secondary dysmenorrhea. The exact prevalence is not known since a laparoscopy is required to make the diagnosis and since the recognition varies with the training and the interest of the laparoscopist. The least-biased estimate for the overall prevalence of endometriosis in reproductive age is about 10% on the basis of a study of women operated on for symptoms other than those associated with endometriosis[5]. Moreover the pathophysiology is poorly understood, which makes it difficult to formulate and test simple hypothesis.

Aetiopathogenesis

According to the Endometriosis Foundation, a woman (or girl) with a mother who has endometriosis is seven times more likely to have the disease herself. Women with short menstrual cycles of less than 27 days, and/or a long menstrual flow of over one week, are

1. Professor & Head. Department of Obstetrics and Gynaecology, Institute of Child and Mother Health
2. Associate Professor Department of Obstetrics and Gynaecology, Institute of Child and Mother Health
3. Assistant Professor Department of Obstetrics and Gynaecology, Institute of Child and Mother Health, Dhaka.

Correspondence to: Professor Nazneen Kabir, Professor and Head, Department of Obstetrics and Gynaecology, Institute of Child and Mother Health, Dhaka. Tel.: +880 1711-563876, e-mail: drnazneendec@yahoo.com

Received 10 November 2014 **Accepted** 02 December 2014

more likely to develop endometriosis. Endometriosis is more common in women with a short menstrual cycle (d"27 days), longer menstrual flow (e"7 days), and spotting before onset of menses[6].

The exact aetiopathogenesis of endometriosis is not known. The main theories for the formation of ectopic endometrium are retrograde menstruation, transplantation, müllerianosis, coelomic metaplasia and metastasis. The theory of retrograde menstruation (also called the *implantation theory* or *transplantation theory*)[7] is the most widely accepted theory for the formation of ectopic endometrium in endometriosis. It suggests that during a woman's menstrual flow, some of the endometrial debris exits the uterus through the fallopian tubes and attaches itself to the peritoneal surface (the lining of the abdominal cavity) where it can proceed to invade the tissue as endometriosis[8]. However, most women have had some retrograde flow, and not all of these women get endometriosis, so there is more to it. The theory of retrograde menstruation as a cause of endometriosis was first proposed by John A. Sampson. Müllerianosis: A competing theory states that cells with the potential to become endometrial are laid down in tracts during embryonic development and organogenesis. These tracts follow the female reproductive (Mullerian) tract as it migrates caudally (downward) at 8–10 weeks of embryonic life. Primitive endometrial cells become dislocated from the migrating uterus and act like seeds or stem cells[9]. Coelomic metaplasia: This theory is based on the fact that coelomic epithelium is the common ancestor of endometrial and peritoneal cells and hypothesizes that later metaplasia (transformation) from one type of cell to the other is possible, perhaps triggered by inflammation[10]. The metastatic theory suggests that ectopic implantation of endometriotic tissue to extra uterine tissue occurs by either lymphatic or hematogenous metastasis explaining its presence in areas outside of the pelvic region, such as in the lungs and arms. In the case being reported upon, the spontaneous umbilical endometriosis could have arisen due to endometrial tissue that is transported via lymphatics or vascular channels[11]. Umbilical endometriosis, also ealled Villar's Nodule, was first described by Villar in 1886. It is extremely rare, the incidence being only 0.5-0.1% of all women with extra gonadal or external endometriosis[12]. There appears to be a genetic link as well. Women with first-degree relatives with endometriosis are predisposed to develop the disease, develop symptoms earlier, and have more severe manifestations[4]. Diet is linked to endometriosis. One study found that there was a 40% decreased risk of endometriosis in women with higher consumption of green vegetables and fresh fruit and an 80% increased risk in women who ate high amounts of beef and other red meats[13].

Some practitioners believe that an overgrowth of yeast has something to do with the initiation and progression of endometriosis evidenced by reversal of symptoms of endometriosis with treatment of *candida*[14]. Some women with endometriosis actually have an allergy to their own hormones, specifically progesterone and LH (luteinizing hormone, which stimulates progesterone production). Following desensitization treatment of endometriosis can be done using progesterone[14].

Dioxins, a by product of many manufacturing processes have long been established as significant hormone disrupters, have an effect like endometriosis[15]. In addition to dioxin, anything that mimics or disrupts normal hormone activity may contribute to endometriosis, such as the phthalates and bisphenols commonly found in plastics, pesticides and insecticides. Even soy, which has estrogen-like properties, may be a problem for women with endometriosis[15].

Signs and symptoms

Clinical presentations of endometriosis are highly diverse. Its main but not universal symptom is pelvic pain. The principle symptoms of the disease include pain, increased volume of the organ and infertility and heavy or irregular bleeding. Other symptoms may include fatigue, painful bowel movements with periods, low back pain with periods, diarrhea and/or constipation and other intestinal symptomps like nausea and vomiting and headache, low-grade fever and hypoglycemia[16]. Some women with endometriosis have no symptoms. Infertility affects about 30-40% of women with endometriosis and is a common result with progression of the disease.

Pain

The most common symptom of endometriosis is pain before and during periods (usually worse than "normal" menstrual cramps), during or after sexual activity. Symptoms of endometriosis-related pain may include[17] dysmenorrhea-painful, sometimes disabling cramps during the menstrual period; pain may get worse over time (progressive pain), also low back pain linked to

the pelvis, chronic pelvic pain– typically accompanied by low back pain or abdominal pain, dyspareunia–painful sex, dysuria–urinary urgency, frequency, and sometimes painful voiding. A major symptom of endometriosis is recurring pelvic pain. The pain can range from mild to severe cramping or stabbing pain that occurs on both sides of the pelvis, in the lower back and rectal area, and even down the legs. Endometriotic lesions react to hormonal stimulation and bleed at the time of menstruation; blood accumulates locally, causes swelling, and triggers inflammatory responses with the activation of cytokines[18]. This process cause pain. Pain can also occur from adhesions (internal scar tissue) binding internal organs to each other, causing organ dislocation. Fallopian tubes, ovaries, the uterus, the bowels, and the bladder can be bound together in ways that are painful on a daily basis, not just during menstrual periods[18]. General pelvic pain may occur when a woman makes a certain movement or sudden actions. This tugging or yanking sensation may result from pulling on adhesions or scar tissues stretching between organs. The location and level of pain may not always directly relate to the extent of visible endometrial growths. Some women with extensive visible endometrial growths may be entirely pain free, while others with a few small growths experience severe pain. Also, endometriotic lesions can develop their own nerve supply, thereby creating a direct and two-way interaction between lesions and the central nervous system, potentially producing a variety of individual differences in pain that can, in some women, become independent of the disease itself[19].

Growth

With endometriosis, abnormal growths occur and proliferate, most typically in the pelvic cavity. Adhesions on the ovaries are common[15]. There may be one or more areas, some as small as a pinhead and others that grow much larger (but rarely larger than an orange). The small areas look like blood blisters and may be blue, dusty red or brownish black, depending on how much fresh or old blood is present[15].

Endometrial cysts may form when ovarian tissue tries to protect itself by growing a "lid" of tissue over the endometrial implant. These cysts swell and bleed cyclically because they respond to hormones and grow like uterine tissue. The cysts may rupture, usually just before or immediately after menstruation, spilling the contents into the pelvic cavity[20].

The swelling and rupture are painful, and the old blood from the cyst is highly irritating to the lining of the pelvic cavity, which causes inflammation and more pain. The cells in the rest of the pelvic area secrete bands of fibrous material that solidify and seal over the ruptured cyst[20]. Repeated spillage from ruptured cysts can produce adhesions that bind the organs together so that the pelvic organs become one large, immovable mass. Endometrial growths can cause obstruction to the bladder or bowel, causing increased constipation in the large bowel, which gets worse at menses. It is often accompanied by a sharp cramp[21].

Localization

The location may not always directly relate to the extent of visible endometrial growths. Some women with extensive visible endometrial growths may be entirely pain free, while others with a few small growths experience severe pain. The most common locations of endometrial growths are in the abdomen-involving the ovaries, fallopian tubes, the ligaments supporting the uterus, the area between the vagina and the rectum, the outer surface of the uterus, and the lining of the pelvic cavity[22]. Sometimes the growths are also found in abdominal surgery scars, on the intestines or in the rectum, on the bladder, lungs, vagina, cervix, and vulva (external genitals). Ureteral or uninary bladder involvement could result in cyclical pain and hematuria during menstruation; Pulmonary involvement could manifest as pneumothorax, hemothorax or hemoptysis during menstruation. External endometriosis, involving the subcutaneous tissues, has also been reported in the vicinity of a surgical scar following surgeries such as hysterectomy, hysterotomy, cesarean section, episiotomy and laparoscopy[23].

Endometriosis may be superficial or deep. Superficial endometriosis does not cause pain and should not be treated by itself; symptomatic relief of pain may be obtained by therapeutic amenorrhea or by the placebo effect of surgery. Deep endometriosis arising under the peritoneal surface is usually located posterior to the vagina and cervix, involving the pouch of Douglas, the rectovaginal septum and the uterosacral liganent[24]. In such cases, pelvic examination shows a painful induration or a nodule in this area. The anterior cul-de-sac and the lateral pelvic wall may also be involved

Staging

It refers to the depth and amount of lesions present. Surgically, endometriosis can be staged I–IV (Revised Classification of the American Society of Reproductive

Medicine)[25]. The process is a complex point system that assesses lesions and adhesions in the pelvic organs, but it is important to note that staging assesses physical disease only, not the level of pain or infertility. A person with Stage I endometriosis may have little disease and severe pain, while a person with Stage IV endometriosis may have severe disease and no pain or vice versa. In principle the various stages show these findings:

Stage I (Minimal)
Findings restricted to only superficial lesions and possibly a few filmy adhesions

Stage II (Mild)
In addition, some deep lesions are present in the cul-de-sac

Stage III (Moderate)
As above, plus presence of endometriomas on the ovary and more adhesions.

Stage IV (Severe)
As above, plus large endometriomas, extensive adhesions.

Endometrioma on the ovary of any significant size (Approximately 2 cm+) must be removed surgically because hormonal treatment alone will not remove the full endometrioma cyst, which can progress to acute pain from the rupturing of the cyst and internal bleeding[26]. Endometrioma is sometimes misdiagnosed as ovarian cysts.

Diagnosis

History and physical examination can lead the health care practitioner to suspect endometriosis. Although doctors can often feel the endometrial growths during a pelvic examination and these symptoms may be signs of endometriosis, diagnosis cannot be confirmed by examination only. Use of pelvic ultrasound may identify large endometriotic cysts (called endometriomas). However, smaller endometriosis implants cannot be visualized with ultrasound technique.

Laparoscopy is the only way to officially diagnose endometriosis as it permits lesion visualization unless the lesion is visible externally, for example, an endometriotic nodule in the vagina. If the growths are not visible, a biopsy may be taken to determine the diagnosis from colour and pain of the lesion[27]. Surgery for diagnosis also allows for surgical treatment of endometriosis at the same time.

To the nacked eye, lesions can appear dark blue, powder-burn black, red, white, yellow, brown or non-pigmented. Lesions vary in size. Some within the pelvic walls may not be visible, as normal-appearing peritoneum of infertility women reveals endometriosis on biopsy in 6-13% of cases[28].

Management

There is no cure of endometriosis but it can be treated in a varietiy of ways like pain medication; hormonal treatment and surgery[29]. In women in the reproductive years, endometriosis is merely managed: the goal is to provide pain relief, to restrict progression of the disease process, and to restore or preserve fertility where needed.

For pain relief nonsteroidal anti-inflammatory drugs (NSAID) and opioids may be used. NSAID injections can be helpful for severe pain or if stomach pain prevents oral NSAID use[30]. Both pregnancy and menopause tend to cause endometrial growths to shrink, so the drugs prescribed typically create a pseudo-pregnancy or pseudo-menopause.

Birth control pills are usually the first course of treatment. However, they typically do not relieve the pain of endometriosis, and they have been identified as a significant contributor to yeast overgrowth. Stronger drugs may be prescribed in more severe cases. Danazol (an androgen similar to testosterone) shrinks and "dries up" the endometrial implants. It also stops ovulation, preventing the egg from bursting out its follicular sac. Without a burst follicle, no progesterone is produced, which prevents the shedding of endometrial tissue. Although considered to be one of the most effective treatments, many of the women who have taken danazol experience a recurrence of the disease within three years[31].

Gonadotropin releasing hormone agonists (GnRH-a), are another type of drugs that suppress hormone production to prevent ovulation and menstruation. Although these drugs appear to have milder side effects than danazol, they have a high rate of recurrence, and typically are not prescribed for more than six months. These drugs are used temporarily to shrink implants prior to surgery (or pregnancy) and sometimes after surgery.

The hormone focus is typically on the imbalance between estrogen and progesterone, but endometriosis sufferers also tend to display disruptions of insulin and glucose. Exaggerated levels of insulin

can actually produce seizures of the fallopian tubes and the gastrointestinal muscles, leading to significant pain. The imbalance of estrogen and progesterone can also influence thyroid activity, potentially adding the symptoms of hypothyroidism to the condition. As such, achieving and maintaining optimal hormone balance can influence the treatment of endometriosis.

Surgical treatment attempts to remove endometrial tissue preserving the ovaries without damaging normal tissue. Conservative surgery consists of the excision of the endometrium, adhesionolysis, resection of endometriomas, and restoration of normal pelvic anatomy as much as possible. The treatment of choice of Villar's Nodule remains surgical excision sparing the umbilicus where possible, and recurenes, though reported, are rare[11]. Malignant transformation of the umbilical nodule into endometrial calcinoma has also been reported[32].

Laparoscopy, besides being used for diagnosis, can also be used to perform surgery to remove all endometriosis and women recover from surgery quicker and have a lower risk of adhesions[33]. 55% to 100% of women develop adhesions following pelvic surgery[34], which can result in infertility, chronic abdominal and pelvic pain, and difficult reoperative surgery. Trehan's temporary ovarian suspension, a technique in which the ovaries are suspended for a week after surgery may be used to reduce the incidence of adhesions after endometriosis surgery[35,36].

Conservative surgery involves excision of endometriosis while preserving the ovaries and uterus, very important for women wishing to conceive, but may increase the risk of recurrence[37]. Recurrence of endometriosis following conservative surgery is estimated as 21.5% at 2 years and 40.50% t 5 years[38]. Hysterectomy (removal of the uterus) can be used to treat endometriosis in women who do not whish to conceive. However, this should only be done when combined with removal of the endometriosis by excision, because if endometriosis is not also removed at the time of hysterectomy, pain may still persist[39]. For women with extreme pain, a presacral neurectomy may be very rarely performed where the nerves to the uterus are cut. However, this technique is almost never used due to the high incidence of associated complications including presacral haematoma and irreversible problems with urination and constipation[39].

Conclusion

Endometriosis is a fairly common but poorly understood disease that is frequently undetected, untreated and misdiagnosed. Despite significant advances in medical diagnostic technology, a confirmatory diagnosis of endometriosis still requires surgical biopsy. This is typically performed by laparoscopy.

References

1. Philippe RK, Ussia A. Epidemiology of endometriosis Gruppo Italo Belga, Rome, Italy. 2003.
2. Maximova Y. Diagnosis: Endometriosis. News from European Medical Center 2012.
3. Endometriosis Association Information. Miracle Babies: Chapter 9 Female Fertility: Clues From Your Past.Copyright 2007 IVF.com, Atlanta, GA, USA.
4. Frackiewicz EJ. Endometriosis: An overview of the disease and its treatment. J Am Pharm Assoc 2000; 40(5):645–57.
5. Wheeler JM. Epidemiology of endometriosis-associated infertility. Reprod Med. 1989; 34(1):41-6.
6. Spaczynski RZ, Duleba AJ. Diagnosis of endometriosis. Semin Repro Med 2003; 21(2):193–207.
7. Saul T, Dave AK. Endometriosis [online article]. Medscape. http:// emedicine. medscape.com/ article/795771-overview. Accessed Nov 12, 2008.
8. Fauser BC, Diedrich K, Bouchard P, Domínguez F, Matzuk M, Franks S, Hamamah S, Simón C, Devroey P, Ezcurra D, Howles CM. Contemporary genetic technologies and female reproduction. Hum Reprod Update 2011; 17 (6): 829–47.
9. Signorile PG, Baldi F, Bussani R, D'Armiento M, De Falco M, Baldi A. Ectopic endometrium in human foetuses is a common event and sustains the theory of müllerianosis in the pathogenesis of endometriosis, a disease that predisposes to cancer. J Exp Clinic Canc Res 2009; 28: 49.
10. Wellbery C. Diagnosis and Treatment of Endometriosis. Am Fam Physician. 1999 Oct 15; 60(6):1753-1762.
11. Victory R. Diamond MP, Johns DA. Villar's Nodule: A case report and systematic review of

endometriosis externa of umbilicus. J Minim Invasive Gynecol 2007; 14:23-32.

12. Purvis RS. Tyring SK. Cutaneous and subcutaneous endometriosis surgical and hormonal therapy. J Dermatol Surg Oncol 1994; 20:693-5.
13. Parazzini F, et al. Selected food intake and risk of endometriosis. Hum Reprod 2004; 19:1755–59.
14. Crook W. The Yeast Connection Handbook Professional Books, Inc.; Jackson, TN; 2002.
15. Lee JR. Natural Progesterone: The Multiple Roles of a Remarkable Hormone. BLL Publishing; Sebastopol, CA. 1993.
16. McCormick K. Endometriosis: *No, Severe pain is NOT "Normal* Women's. International Pharmacy | Madison, WI 53718 | Youngtown, AZ 85363. February 2013.
17. Ballweg ML. Endometriosis: The Complete Reference for Taking Charge of Your Health, the Endometriosis Association. McGraw-Hill; 2004 New York, NY.
18. Murray, Michael T, Joseph P. (The Encyclopedia of Natural Medicine (3rd ed.). Simon and Schuster New York, NY: 2012.
19. WhealerJM, Malinak LR. Recurrent Endometriosis, Contrib Gynaecol Obstet 1987; 16:13-21.
20. Endometriosis; NIH Pub. No. 02-2413; September 2002
21. Van der Linden PJ. Theories on the pathogenesis of endometriosis. Hum reprod (Oxford, England). 1996; 11 Suppl 3: 53–65.
22. Stratton P, Berkley KJ. Chronic pelvic pain and endometriosis: translational evidence of the relationship and implications. Hum Reprod Update 2011; 17(3):327
23. Albrecht LE, Tron V, Rivers JK. Cutaneous endometriosis. Int J Dermatol 1995; 34:261-2.
24. Querleu D. Pelvic pain and external endometriosis Physiopathology and treatment. Contracept Fertil Sex. 1995; 23(1):29-36.
25. Revised American Society for Reproductive Medicine classification of endometriosis: Fertility and Sterility 1996; 67(5):817–21.
26. Anisah J. Management of ednometriosis. Education, Health & Medicine obsgynhsnz (16 SlideShares) Published on Sep 21, 2013.
27. Demco L. Mapping the source and character of pain due to endometriosis by patient-assisted laparoscopy. J Am Assoc Gynecol Laparosc. 1998; 5(3):241-5.
28. Office on Women's Health, US Department of Health and Human Service. (16 July 2012). Endometriosis Fact Sheet. Ratrieved from Womens health. gov.
29. Nisolle M. Paindaveine B, Bourdon A, Berliere M, Casanas-Roux F, Donnez J Histologic study of peritoneal endometriosis in infertile women. Fertility and Sterility 1990; 53(6): 984-8.
30. Olive DL, Schwartz LB. Endometriosis. N Engl J Med. 1993; 328(24):1759–1769.
31. Farquhar C. Endometriosis: A Clinical review. BMJ 2007; 334: 249-53.
32. Sonavane SK. Kantawala KP. Menias CO. Beyond the boundaries endometriosis: typical and atypical locations. Curr Probl Diagn Radiol. 2011; 40(6):219-32.
33. Endometriosis and Infertility: Can Surgery Help. American Society for Reproductive Medicine. 2008. Retrived 31 Oct 2010.
34. Liakakos T, Thomakos N, Fine PM, Dervenis C, Young RL. Peritoneal Adhesions: Etiology, Pathophysiology, and Clinical Significance. Dig Surgery 2001; 18(4): 260-73.
35. Trehan AK. Temporary ovarian suspension. Gynaecol Endos 2002; 11(1):309-314.
36. Abuzeid MI, Ashraf M, Shamma FN. Temorary ovarian suspension at laparoscopy for prevention of adhesions. J Am Assoc Gynecol Laparosc 2002; 9(11):98-102.
37. Namnoum AB, Hickman TN, Goodman SB, Gehlbach DL, Rock JA. Incidence of symptom recurrence after hysterectomy for endometriosis. Fertility and Sterillity 1995; 64(5):898-902.
38. Gou SW. Recurrence of endometriosis and its control. Hum. Reprod Update 2009; 15(4):441-61.
39. Johnson NP, Hummelshoj L. Consensus on current management of endometriosis. Hum Reprod Update 2013; 28(6):1552-68.