Endometriosis

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Abstract

Endometriosis is a common condition in women of childbearing age that has the potential to significantly impact on a woman's quality of life, ability to work and fertility. An awareness of the condition, and understanding of the current literature, is important in being able to provide appropriate, individualized care to patients. This review provides a background on all aspects of endometriosis, including radiological investigations, surgical management and the role of specialist Endometriosis centres.

Keywords deep infiltrating endometriosis; endometriomas; endometriosis; endometriosis/complications; endometriosis/diagnosis; endometriosis/surgery; magnetic reasonance imaging; rectal diseases/pathology; rectovaginal endometriotic nodule; urinary tract endometriosis

Introduction

Endometriosis is an oestrogen-dependent, chronic inflammatory condition characterized by the presence of functional endometrial glands and stroma outside the uterine cavity. Bleeding, inflammation, fibrosis and adhesion formation result from the ectopic tissue and, while the most commonly affected site remains the pelvis, distant sites can be involved and may mimic other disease processes. The condition has an estimated prevalence of 5–10% in women of childbearing age, with peak incidence between 25 and 35 years old. However, it may also affect younger women presenting with chronic pelvic pain. The prevalence amongst infertile women is between 30 and 50%. Endometriosis can be a debilitating condition with impact on quality of life, relationships and reduced earning capacity. The EndoCost study demonstrated it costs the UK economy £8.2 billion a year in treatment, loss of work and healthcare costs.

Risk factors and genetics

There are several risk factors associated with endometriosis (Box 1). The current trend towards earlier menarche and delayed age of childbirth lead to increased number of ovulations and menstrual cycles; with regular menstrual flows increasing the risk of endometriosis.

Endometriosis may vary with ethnicity, with higher prevalence amongst Asian women and lower incidence among African women, when compared to Caucasians. These ethnic variations indicate the significance of genetic and environmental risk factors.

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Risk factors for endometriosis

- Early menarche
- Short menstrual cycle
- Prolonged/heavy menstrual flow
- Delay of first birth
- Reduced number of pregnancies
- Positive family history

Box 1

The genetic element of endometriosis is firmly established and remains a research focus. The estimated heritability is 51%. A locus on chromosome 7p15.2 is currently linked with endometriosis in women of European ancestry, with higher genetic propensity towards moderate-severe disease. The genes WNT4, CDKN2B-AS1 and GREB-1 are also implicated, for their roles in development of the female reproductive tract, tumour suppressor proteins and estrogen receptor-regulated pathways respectively.

A genetic basis for developing endometriosis is supported by reports of familial aggregation, with high risk of endometriosis in those with an affected first-degree relative and observations of concordance of endometriosis in twins.

Aetiology

Are we any closer to the answer?

The clinical manifestation of endometriosis and presence of endometrial tissue outside the uterine cavity is likely the end point of a combination of several aberrant biological processes. Many theories exist about the aetiology, but a single, definitive mechanism has yet to be agreed. The most commonly cited theory to explain peritoneal endometriotic lesions is Sampson's Retrograde Transplantation Theory. This suggests endometrial cells are driven through the fallopian tubes, via reflux action during menstruation, and are deposited in the pelvis where they invade serosal surfaces. While we know that up to 90% of women can have retrograde menstruation, only 15% of women with retrograde flow actually have endometriosis. In fact, there is no in vivo or in vitro evidence that endometrial cells in peritoneal fluid can attach or invade peritoneal surfaces. This theory also fails to account for why endometriosis can be found at distant sites, in pre-pubertal girls and in men. However, a similarity has been observed between ectopic endometrial lesions and the basalis layer of uterine endometrium, supporting the possibility of retrograde menstruation providing a route for endometrial stem cells to extrauterine structures.

This Coelomic Metaplasia Theory suggests endometriosis develops from metaplastic transformation of cells lining the visceral/abdominal peritoneum into endometrium. The trigger for metaplasia is an undetermined stimulus, potentially hormonal, infectious, or environmental. Proponents of this theory believe spread to distant sites may occur through lymphatic or haematogenous spread, or iatrogenically during surgery. Given the shared embryological origin of pelvic, abdominal and thoracic tissues, this theory offers reasonable explanation for endometriosis. However, ageing tissues also undergo metaplasia, therefore increased incidence of endometriosis should also occur with increasing age.

The most plausible explanation for endometriosis is the embryological Mullerianosis Theory. This postulates that if the basis of endometriosis is an alteration of genital tract structures during organogenesis, it should be possible to see misplaced endometrial tissue outside the uterine cavity of female human foetuses at autopsy. In a study by Signorile at al (2009) involving 36 foetuses, with no anatomical genital tract abnormalities, four foetuses were found to have primitive endometrium outside the uterine cavity, expressing oestrogen and CA125 receptors. This 11% correlates well with the reported adult prevalence of endometriosis and the fact that low recurrence rates exist after complete surgical excision of endometriosis. Some of the other theories in the literature are summarized in Table 1.

Presentation

Asking the right questions is key

On average it takes 7.5 years from onset of symptoms to confirm a diagnosis of endometriosis. Pain, in the form of dysmenorrhoea, generalized pelvic pain and deep dyspareunia are among the most common presenting symptoms to general gynaecology clinics. Other features include infertility, often coexisting with bowel/bladder symptoms, back pain, low mood, reduced quality of life and fatigue (secondary to chronic pain). It has been reported that more than 50% of patients with deep infiltrating endometriosis (DIE) actually present with associated symptoms of dyschezia and dysuria. Up to 20% of women with endometriosis have concurrent irritable bowel syndrome, interstitial cystitis and migraines. Given the genetic basis of endometriosis, a family history should also be explored. Taking a targeted history is imperative and will often enable a good clinician to judge, prior to diagnostic laparoscopy, the likelihood of identifying disease.

Be on the look out for signs

Following the history, a bimanual and speculum examination should be performed. While many cases of endometriosis may be associated with a paucity of findings, other pathology can be excluded. It can be easy to miss subtle signs of endometriosis, including discrete nodules and tenderness in the posterior fornix, uterine motion tenderness or palpable thickening of the uterosacral ligaments. The cervix can also be laterally displaced if there is unilateral uterosacral thickening/shortening. Occasionally, lesions may be visible in the vaginal mucosa or cervix. Suspicion of severe disease should be raised if the uterus is immobile or very retroverted. An endometrioma may be detected through palpation of a tender, adnexal mass.

Other aetiologies for Endometriosis

Theory	Overview
Immune dysfunction	Autoimmune disease more common in women with endometriosis. Defective immune response in elimination of menstrual debris, promotion of ectopic endometrium secondary to inflammation.
Oxidative stress	Immune cells produce cytokines promoting endometrial growth + angiogenesis. Women with endometriosis have higher levels of cytokines/vascular endothelial growth factors in peritoneal fluid.
Stem cells	Undifferentiated stem cells with ability to regenerate into endometriotic deposits.

Table 1

Diagnosis

The gold standard

The leading investigation to confirm endometriosis is a diagnostic laparoscopy. This should be performed systematically, inspecting the ovaries, tubes, ovarian fossae, uterosacral ligaments, Pouch of Douglas (POD), uterovesical fold, rectosigmoid and appendix. Adhesions and pelvic mobility should also be noted. The operation report should describe the size, macroscopic appearance, location and depth of infiltration for all lesions. Images should be taken to facilitate optimal record keeping, patient education and referral to an endometriosis specialist where required. While endometriosis is considered a histological diagnosis, biopsies are rarely necessary during diagnostic procedures. Surgical experience is key in ensuring a correct diagnosis of endometriosis from visual inspection alone, with reported sensitivity of 94–97% and specificity of 77–85%.

If endometriosis is identified, which requires surgical management and has greater operative risk, patients should be fully counselled and re-listed at a later date. Contrary to some schools of thought, it is our experience that diagnostic procedures ± diathermy treatment to endometriosis is ineffective. Minor treatment to superficial disease is likely to offer short-term symptom management only, leading to the potential for repeated diagnostic procedures, and increased risk of adhesions. It also results in a failure to diagnose other causes of pain. Minor treatment to DIE is an ineffective measure, and patients should be referred to specialist centres to discuss formal excision.

What are we looking out for?

The appearances of endometriotic implants are highly variable. Superficial disease appears as patches of either blue/black 'powder burn', flame red or clear vesicles (Figure 1). DIE is represented by thick nodules, plaques, peritoneal tethering or an obliterated POD. Associated anatomical distortion should be evaluated, including relationship of the ureters and rectosigmoid to any deep nodules.

Clinical markers

There are no clinically useful serum markers to diagnose or monitor disease activity in endometriosis. While CA125 can be raised in severe disease, it lacks sensitivity and is not routinely used. Peritoneal markers have been proposed, but these are subject to cyclical variations and none yet exist with enough specificity to correlate with endometriosis alone. Other studies have investigated the role of endometrial biopsy/immunohistochemical staining, to detect increased numbers of unmyelinated, sensory C fibres in women with endometriosis. Limitations exist in interpreting how this relates to pain symptoms, although a recent report indicates presence of nerve fibres positively correlates with pain severity.