

Diagnosing Endometriosis Through Imaging

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Abstract: Endometriosis is a complex disease affecting many women throughout the world. There is currently no cure, just treatments that may help alleviate symptoms. Diagnostic imaging is proven to help detect endometriosis in women suffering from the disease and can help locate atypical lesions. This leads to an increase in diagnosis time and improves laparoscopic surgeries as surgeons will have a better idea of where to look to remove the endometriomas.

Chronic pelvic pain, infertility, painful intercourse, fatigue, excessive bleeding, painful bowel movements, pain with urination, nausea and constant bloating are just some of the symptoms of endometriosis. Approximately 176 million women in the world suffer from this disease. This illness is not well known to many women and health care workers which make diagnosing this condition difficult. The average time it takes for a woman to be diagnosed with endometriosis is six to ten years. There is currently no known cure, only treatments that can help alleviate symptoms. The main indications of endometriosis include painful menstruation which can be mild or debilitating, infertility, painful intercourse and digestive problems. Women may experience all of these symptoms or none as every woman presents different ailments. Endometriosis is found predominantly in women of child-bearing age and is most often diagnosed in women in their thirties; however, it can be diagnosed in women in their teens who have chronic pelvic pain and painful menstruation. There are some factors that increase your chance of having endometriosis. These include increased exposure to menstruation, having an early age of menarche, short menstrual cycle, long duration of menstrual flow, and positive family history.² There are several theories on why endometriosis forms, and the most widely accepted is the metastatic theory, which holds that endometrial cells and stroma implant in ectopic locations within the pelvis, most likely secondary to retrograde menstruation.² Once endometriosis is transported, the endometrial cells implant on the serosal surfaces and remain viable. An alternative theory is the coelomic theory, which states that endometriosis develops from metaplastic transformation of cells lining the pelvic peritoneum since both endometrial and peritoneal cells derive from the coelomic wall epithium.² Endometriosis is most commonly found in the ovaries first, then uterine ligaments, serosal surfaces, cul-de-sac, fallopian tubes, rectosigmoid, and urinary bladder. It may also be found in more places within the body with

stage four or five endometriosis. The prevalence of endometriosis has been found to be significantly higher in women who are infertile than in women who are fertile.³ Every woman experience differentiating pain due to endometriosis as each case varies on severity and prevalent symptoms.

The Different Stages and Symptoms of Endometriosis

Endometriosis can be classified into four different stages. The American Society of Reproductive Medicine created a point system to help determine which stage of endometriosis a woman may be in. They are classified by the degree of lesions found, depth and endometrial implants discovered. However, the stages do not determine how severe their symptoms may be, as a woman with stage one endometriosis may experience more pain than a woman with stage five endometriosis. Stage one is between one and five points, it includes minimal lesions and few superficial implants. This is where the peritoneum starts becoming infiltrated with endometrial tissue.³ This stage is hard to see on ultrasound, MR or CT imaging, therefore it is harder to diagnose. Stage two is between 6 and 15 points, it involves a mild number of lesions and deeper implants. It is seen that the endometrium is established within the ovaries and chocolate cysts are found.³ These cysts are concerning due to their ability to spread endometriosis quickly. If the cysts break, it can begin spreading the disease into the pelvic cavity and it will be even more difficult to stop the spread. Stage three is between 16 and 40 points and is classified as moderate lesions, with many deep implants, small cysts on one or both ovaries, and a presence of filmy adhesions.³ In this stage, endometriosis begins an increase in spreading to the pelvic organs such as the ovaries, rectum and uterus. Lastly, stage five is the most severe with greater than 40 points. It contains many deep implants, large cysts on one or both ovaries, and many dense adhesions. Endometriosis can be found on the organs within the pelvic region and outside of it.

Some organs where lesions may be found are the bowels, appendix, diaphragm, heart, lungs, and even brain. Although most women have reflux menstruation, only about 10% of them develop endometriosis.³ However, a subset of women with müllerian duct anomalies, that cause obstruction of antegrade menstruation, are considered to have an increased risk for endometriosis.⁴ Women with this disease are also at risk for developing both clear cell and endometrioid subtypes of epithelial ovarian cancer. An estimated 2.5% of women with endometriosis develop ovarian cancer.⁴ Women with endometriosis-associated ovarian cancer have a better prognosis than woman with ovarian cancer but no endometriosis. This is due because women in the former group tend to develop lower grade tumors that manifest at an earlier stage.⁴ The human epididymal secretory protein E4 level is elevated in women with either endometriosis-associated or conventional ovarian cancer, but not in women with benign endometriosis.⁴ It is important for women suffering from endometriosis with worsening or new symptoms to be checked for this protein to catch the possibility of ovarian cancer sooner.

Laparoscopic Procedures

Furthermore, the different stages of endometriosis require unique treatment planning, imaging, and diagnosing. Laparoscopy is the standard of reference for the diagnosis and best treatment method for endometriosis. The look of typical lesions found during a laparoscopic surgery consist of brown or black nodules or plaques on peritoneal surfaces and are pathognomonic.² It is extremely difficult to see mild endometriosis through imaging modalities such as (US), CT, and MRI. The only way to be completely sure is to have a diagnostic laparoscopic surgery to take a sample of the tissue or lesion to test for endometrioses and clean out the lesions or masses found. Since this is a more invasive surgery, doctors often have patients

try other avenues first to diagnose and treat endometriosis. This is where imaging modalities and medication treatments come in to play.

Ultrasound and Endometriosis

Ultrasound is usually the first route women will go for imaging of endometriosis. This is for various reasons. One being it is a cheaper, more readily available scan compared to an MRI or CT. A negativity when it comes to ultrasound is it is incredibly hard to see endometriosis in stage one, two and even three because the lesions are not large enough to be distinguishable.

Ultrasound can be very useful for seeing later stage endometriosis because it can pick up on large lesions and cysts in the pelvic organs and bladder. Ultrasound can also help diagnose deep nodules or masses in the rectovaginal septum or other areas. Endometriosis is most commonly found in the ovaries and pelvic peritoneum which makes imaging these areas important.

Sonographers can image the ovaries well which makes it easier to diagnose if there is presence of endometriosis on one or both ovaries and the stage of lesions found. One big sign of ovarian endometriosis seen during an ultrasound is “kissing” ovaries. This is where ovaries are adherent to one another posterior to the uterus and is frequently seen with bilateral endometriomas.⁵ The classic appearance of an endometrioma, is often referred to as a “chocolate cyst” because of the presence of thick, dark, degenerated blood products within the endometrioma and cysts.²

Endometriomas are a homogeneous, hypoechoic lesion within the ovary with low-level echoes and no internal blood flow, which differentiates them from other lesions during an ultrasound.² It is important for radiologists to be able to tell the difference between a common cyst and a chocolate cyst so women can get the proper treatment. Chocolate cysts will not go away over time like normal, fluid filled cysts that will dissipate.

Transrectal ultrasound may be useful imaging to see if endometriosis is present in the rectum and to detect lesions on the posterior bladder wall. The appearance of nodules can be varied. It includes hypoechoic linear or spherical lesions, with or without regular contours involving the muscularis (most common) or (sub)mucosa of the bladder.⁵ Nodules of endometriosis tend to appear as solid, hypoechoic, irregular masses on sonography images. These nodules may contain echogenic foci or small cystic spaces and often show little or no blood flow on color doppler.⁵ Rectal endoscopic sonography uses a higher frequency and radial probes which allows better evaluation and visualizes the diameter of the lesions seen. Although enteroclysis is rarely performed because small-bowel endometriosis is rare, it is suitable for radiographic visualization of extrinsic infiltrative involvement of small-bowel endometriosis². It is important the entire bowel is imaged and not just the affected area. If any portion is missed, it will be extremely difficult to completely remove the lesions during a laparoscopic procedure and the patient's pain will not go away.

When performing transvaginal sonography, bowel nodules can appear as atypical masses on the intestinal wall. A study demonstrated that using transvaginal sonography with water as a contrast agent in the rectum showed a sensitivity of 97% for identifying rectovaginal endometriosis; identification of infiltration into the muscular layer of the rectum was also improved.² Transvaginal ultrasound can be used to detect endometriosis in the bladder. When performing the ultrasound on the bladder, sonographers may notice nodular formations in the vesicouterine pouch, that may or may not contain cysts.³ These nodules can implant on the adventitial layer of the ureter and may also invade the muscularis layer, causing hyperplasia and fibrosis which may lead to a ureteric stricture resulting in hydronephrosis.³ Women may also

notice other symptoms of bladder endometriosis, such as frequent urination and pain or blood when urinating.

MR Imaging and Endometriosis

The next best imaging modality to detect endometriosis is a magnetic resonance imaging (MRI). This scan helps guide surgical approaches to treating endometriosis and can provide better imaging of what organs are affected by the disease. MRI is a non-invasive, non-ionizing radiation method that offers high contrast resolution. This allows multiplanar evaluation of endometriosis, thus facilitating a correct diagnosis and appropriate treatment.⁶ It is extremely helpful to visualize deep infiltrating lesions and masses, and to see unusual sights within the body lesions have infiltrated, such as the diaphragm or bowels. Radiologists must be familiar with the MR imaging appearances of endometriosis in order to guide clinicians and provide adequate information to assure accurate diagnosis and timely treatment of its entity.⁶ An MRI is also superior for diagnosing rectosigmoid lesions and endometriosis of the bladder. During an MRI, a T-1 weighted fat-suppressed sequence increases the detection of small implants. The increase in awareness allows better definition as well as differentiation between hemorrhagic and fat components contrast-enhanced sequences. This is useful for detection of microscopic endometrial implants associated with inflammatory reaction, as well as assessing for malignant change.⁴ The classic endometrioma look on a MR image shows shading, defined as a range of low-signal intensities on T2-weighted images and a corresponding high signal on T1-weighted images⁴. This shading reflects the chronic nature of the endometrioma resulting from repeated episodes of hemorrhage accumulating over months and years with extremely high concentrations of iron, protein, and intracellular methemoglobin.⁴ With endometriosis, there can be involvement of the uterine ligaments, especially the uterosacral ligaments. These nodules lead to thickening

and, in later stages, to fibrosis and adhesions causing cul-de-sac obliteration.⁶ In MR imaging, adhesions usually have low signal intensity and obscure parts of organs they are adhered to. The presence of adhesions may be suggested by posterior displacement of the uterus and ovaries, angulation of bowel loops, elevation of the posterior vaginal fornix, and loculated fluid².

While MRI is useful for detecting endometriosis in the ovaries and uterus, it has a low sensitivity (33%) for detecting rectal lesions due to artifacts related to rectal content.⁵ To increase the

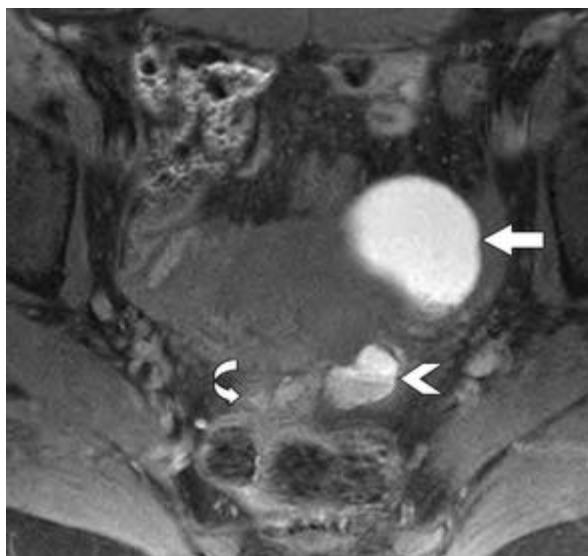


Figure 1: Demonstrates left ovarian endometrium during an MRI scan²

visualization of rectal lesions, MRI sensitivity can be increased in a few different methods. The procedures include the use of water enema, endovaginal coils and phased array coils.⁵

Techniques are being invented every day to help increase the quality of images taken on patients suffering from endometriosis in hard to see places.

Endometriotic implants affect the urinary tract in up to 20% of cases and can be incredibly painful and uncomfortable for women.² The bladder is involved in most cases, followed by the distal ureters, the kidney, and the urethra. Menstrual hematuria is seen in only 20 to 30% of patients with endometriosis in the urinary tract.⁶ The masses are typically near the dome of the bladder and are often confined to the serosal surface; however, they can infiltrate the muscle and appear as mural masses projecting into the bladder lumen.² In one case series involving 20 women who underwent surgical resection of bladder endometriosis, 19 had disease of the posterior bladder wall with direct extension that either partially or completely obliterated

the vesicouterine pouch (also known as the anterior cul-de-sac).⁴ Patients with endometriosis involving the bladder usually present with nonspecific symptoms. This includes frequent urination, burning sensation when urinating, and pelvic pain. These are all symptoms of other ailments such as urinary tract infections which makes it even harder to diagnose and treat.

Many women suffer from infertility that is caused by complications with endometriosis. Approximately 28% of women with endometriosis have abnormalities of the fallopian tubes identified at hysterosalpingography.² Many women first discover they have endometriosis when they are struggling with conceiving. This puts the average age of a woman being diagnosed with endometriosis in their early thirties, after they have possibly suffered from the disease for years. Endometriosis may cause the fallopian tubes to become dilated which may be the only finding of endometriosis in an MRI scan for some women.⁴ In women with endometriosis and a dilated fallopian tube, approximately 40% of the tubes had T1-hyperintense contents, whereas 60% had imaging features suggestive of a simple hydrosalpinx.⁴ This can cause the fallopian tube to become blocked and make it difficult for women to become pregnant. The patient would have to have a procedure to clear out the fallopian tubes to try and reopen the blocked areas and remove the excess tissue.

Solid endometriosis, which is also referred to as deep pelvic endometriosis or deeply infiltrative endometriosis, is defined by the extension of endometrial glands and stroma at least 5 millimeters beneath the peritoneal surface.⁶ Unlike endometriomas, which contain

viscousproteinaceous and hemorrhagic contents, solid masses are composed of ectopic endometrial gland and stromal cells embedded within dense fibrous tissue and smooth muscle.⁴ One of the most commonly encountered locations of solid invasive endometriosis is the rectouterine pouch, or posterior cul-de-sac and the uterosacral ligaments. The ligaments are located near the large intestine and the cul-de-sac can be found between the bladder and uterus. The cul-de-sac is commonly overlooked when getting a laparoscopic

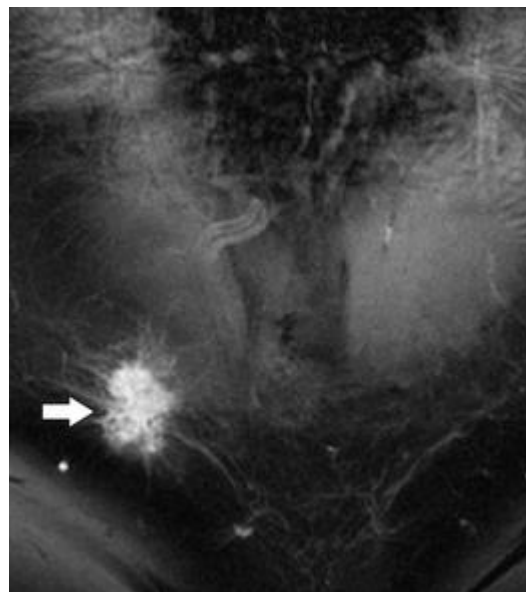


Figure 2: Demonstrates an MRI view of an endometrioma that was palpable during examination²

surgery but is a very important location to check during the procedure to properly treat the disease. Solid endometriosis in this site often extends to or invades the posterior myometrium.⁴ Invasive, solid endometriosis that involves the uterus is an “outside-in” process that often spares the uterine junctional zone. It should not be misclassified as adenomyosis.⁴ Women with a uterus in anteflexion (long axis of the body of the uterus is bent forward on the long axis of the vagina at the internal os) are more likely to develop solid endometriosis of the anterior compartment. While women with a uterus in retroflexion (the top of the uterus points towards the back of the pelvic region rather than tilting towards the bladder) are more likely to develop posterior compartment endometriosis. These findings support the hypothesis that retrograde menstruation contributes to the early pathogenesis of endometriosis.⁴ Some symptoms women may experience are pelvic pain, chronic cramping, and gas pain. Routine MR imaging has a reported sensitivity of 69% and a specificity of more than 90% for the diagnosis of uterosacral ligament

endometriosis.⁴ In one study, MRI was even more accurate than both endovaginal and endorectal ultrasound. When women undergo MR imaging for suspected deep pelvic endometriosis, some investigators advocate distention of the vagina, rectum, or both with sterile gel to obtain better definition of the posterior cul-de-sac, the anterior rectosigmoid colon, and the uterosacral ligaments.⁴ It is important to get the best imaging available to properly treat these deep pelvic lesions to decrease the spread and pain women go through.

MR imaging is useful for evaluating suspected uterine anomalies in women. If there is an obstruction, MR imaging can be used to localize it, determine which segments of the reproductive tract are distended with blood, and determine whether endometriomas and other manifestations of endometriosis are present.⁴ During MR imaging of the bladder, uterine adenomyosis appears as poorly margined tissue with low T2 signal intensity and variable internal 1–4-mm foci with high T2 signal intensity.⁴ Patients may benefit from both ultrasound and MR imaging of the bladder to get a whole picture of how much of the bladder is affected by endometriosis.

Bowel endometriotic implants are estimated to occur in 12–37% of patients with endometriosis.² Commonly affected areas include the rectosigmoid colon, appendix, cecum, and distal ileum. The diagnosis of bowel endometriosis is challenging. US, double-contrast barium enema, CT, and MRI have all been used, but all imaging techniques have limitations.⁴ Bowel involvement is diagnosed on MRI when retractable nodular formations, which are



Figure 3: Demonstrates bowel endometriosis during a barium enema lateral projection

hypointense on T2-weighted images, are found adhering to the wall.² The rectosigmoid colon is the intestinal segment most commonly involved in bowel endometriosis. Completing a double-contrast barium enema examination may demonstrate the presence of extrinsic mass in association of the bowel wall and is highly suggestive of endometriosis, particularly when observed in the rectosigmoid colon.² Endometriosis in the bowel may mimic other intestinal diseases that cause abdominal pain such as bowel perforation, obstruction, and rectal bleeding, which often leads to a delay in diagnosis. Endometriosis is often confused with Crohn's disease because both involve problems within the bowel and there may be transmural extension of inflammation leading to formation of strictures, adhesions, fibrosis, and obstruction.² Women with symptoms specific to rectosigmoid involvement often benefit from resection of serosa-based lesions. When there is a deep invasion of the muscularis propria, complete surgical resection of the affected bowel segment may be performed.⁴ During surgical resection, most endometrial lesions that have penetrated the muscularis propria and invaded the submucosa are found to involve at least 40% of the circumference of the rectal wall.⁴ The MR imaging features of solid rectosigmoid endometriosis have been described as including a “mushroom cap” sign, which is considered a specific finding of solid invasive endometriosis of the rectosigmoid colon on T2-weighted MR images.⁴

Cesarian scars and other abdominal scars may be an uncommon site where endometriosis appears. In MR imaging, these masses appear similar to solid endometriosis at other sites.⁴ Women may present with palpable masses within laparoscopy incisions, and other abdominal incisions, especially cesarean delivery scars.⁴ The occurrence of solid endometriosis in these locations is hypothesized to be independent of retrograde menstruation.⁴ Direct implantation of endometrial glands and stroma during cesarean delivery or a laparoscopic procedure (typically a

myomectomy) is thought to be the cause.⁴ In one surgical case series involving 40 women with solid endometriosis of the abdominal wall, the presence of endometriosis was known preoperatively in fewer than half of the women.⁴ This study shows how common it is for women to go years without diagnosis and the importance of awareness with this disease to help women get treatment sooner before it forms masses.

Malignant transformation is an extremely rare complication of endometriosis. Approximately 75% of malignant transformations arise from the ovary.⁴ Other less common sites include the rectovaginal septum, rectum, and sigmoid colon. Most common histopathologic subtypes arising in ovarian endometriomas are the endometrioid and clear cell carcinoma.⁴ During an MRI, an enhancing mural nodule on T1-weighted gadolinium-enhanced sequences is the most common imaging appearance.² Despite the advantages of MRI over the other imaging modalities, it still has multiple limitations, such as difficulties detecting small lesions and the possibility of anatomy obscuring the view of endometrial masses. There is room for improvement with the imaging of endometriosis in MRI, but it has come a long way and is improving daily.

Medication Treatment for Endometriosis

Many doctors prefer to treat women suffering from endometriosis symptoms with different types of hormonal therapy before performing a laparoscopic surgery or imaging. Treatment therapies include birth control, Intrauterine devices (IUD), Gonadotropin-releasing hormone (Gn-RH) agonists and antagonists' drugs. These drugs block the production of ovarian-stimulating hormones, lowering estrogen levels and preventing menstruation in which case causes the endometrial tissue to shrink.⁸ All of these hormonal treatments can help slow down the spread of endometriosis but will not stop the disease all together or the pain that goes with it.

Some doctors even suggest getting pregnant to help with the symptoms. Surgeons will not perform a laparoscopic surgery until the patient is having difficulties becoming pregnant. If the doctor decides to perform a laparoscopic surgery, it is very important to have a surgeon familiar with endometriosis and the different ways it can appear in order to completely remove it all. If sections are missed, no matter how small, the pain will not go away, and endometriosis will continue to spread. Even if all of the lesions and endometriomas are removed, it can still come back, and many women will be required to have more than one laparoscopic surgery in their lifetime. It is common for women to have the surgery every few years until a hysterectomy has been decided to be performed. Although studies have shown endometriosis lesions returning even after having a total hysterectomy and pain still being prevalent, many women still choose to have a hysterectomy. Even after entering menopause, symptoms will continue until those implants and lesions are removed. Treatment plans will vary by patient and what might work for one woman will not work for the other. Many women still suffer daily from the effects of the disease even while getting some type of treatment. There is still a lot to learn when it comes to best treating someone suffering from the disease. The best thing a woman can do while suffering from endometriosis is research the disease and the different treatments available to them, and if possible, go to an endometriosis specialist.

Conclusion

In conclusion, endometriosis is a complex disease that requires multiple treatment avenues. Currently, laparoscopic surgery is the best method for treatment and removal of endometriosis, but ultrasound and MR imaging may be a great tool in discovering and mapping out treatment plans for women suffering from this disease. In the coming years, science may advance and make imaging of higher quality. This will help women get diagnosed with

endometriosis sooner, lessening the uncertainty, pain, and frustrations many women deal with for years before getting proper treatment. Chances are, you may know someone suffering silently from this disease that do not know where to go for help. It is important to spread awareness so these women do not have to suffer as long and can get the treatment they need. Together we can decrease the diagnosis time of endometriosis and improve women's health across the world.

Resources

1. Endometriosis.org. 2021. *Facts About Endometriosis* « *Endometriosis.Org*. [online] Available at: <<http://endometriosis.org/resources/articles/facts-about-endometriosis/>> [Accessed 6 January 2021].
2. Foti PV, Farina R, Palmucci S, et al. Endometriosis: clinical features, MR imaging findings and pathologic correlation. *Insights Imaging*. 2018;9(2):149-172.
3. Choudhary S, Fasih N, Papadatos D, Surabhi VR. Unusual imaging appearances of endometriosis. *AJR Am J Roentgenol*. 2009;192(6):1632-1644.
4. Bennett GL, Slywotzky CM, Cantera M, Hecht EM. Unusual manifestations and complications of endometriosis--spectrum of imaging findings: pictorial review. *AJR Am J Roentgenol*. 2010;194(6 Suppl):WS34-46.
5. Siegelman ES, Oliver ER. MR imaging of endometriosis: ten imaging pearls. *Radiographics*. 2012;32(6):1675-1691.
6. Yang, N., 2021. *Endometriosis | Radiology Reference Article | Radiopaedia.Org*. [online] Radiopaedia.org. Available at: <<https://radiopaedia.org/articles/endometriosis>> [Accessed 6 January 2021].
7. HSU, A., KHACHIKYAN, I. and STRATTON, P., 2021. *Invasive And Noninvasive Methods For The Diagnosis Of Endometriosis*. *Clin Obstet Gynecol*. 2010;53(2):413-419
8. MayoClinic.org. 2020. *Endometriosis - Diagnosis and Treatment - Mayo Clinic*. [online] Available at: <<https://www.mayoclinic.org/diseases-conditions/endometriosis/diagnosis-treatment/drc-20354661>>. [Accessed November 18, 2020].