Endometriosis: Radiologic evaluation with magnetic resonance

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Learning objectives

Briefly review the epidemiology, pathogenesis and clinical features of endometriosis, as well as its complications.

Discuss MR imaging protocol in patients with suspected or already diagnosed endometriosis.

Present the most common manifestations of pelvic endometriosis at MR imaging, illustrating some of them with images collected over a 4-year period (from June 2010 to June 2014) in our institution.

Recollect the imaging features in magnetic resonance that allow distinction between endometriotic lesions and other pelvic masses.
Background

Endometriosis is a disease characterized by the presence of functional endometrial glands and stroma outside the uterine cavity - the so called ectopic endometrium.

This disorder affects mainly women of reproductive age, mean age at diagnosis being approximately 25-29 years old. However, it is also frequent among adolescents, affecting about half of symptomatic women under 20 years of age with chronic pelvic pain or dyspareunia, main cause in this age group being obstructive müllerian duct anomalies of the cervix or vagina. Only about 5% of cases of endometriosis occur in postmenopausal women, usually associated with exogenous estrogen replacement therapy, and cases in men are quite rare, also related to long-term estrogen therapy (for example related to the treatment of prostate carcinoma).

An ancient classification divided endometriosis into endometriosis interna (referring to endometrial cells within the myometrium) and endometriosis externa (referring to endometrial cells in other sites).

Currently, endometriosis interna has been replaced by the term adenomyosis and endometriosis externa is generally called endometriosis.

Endometriosis is a complex condition, whose pathogenesis is still under discussion and is most probably based on multifactorial causes. Three main theories have been suggested in order to try to explain the histogenesis of this disease:

1) Retrograde menstruation with implantation of endometrial tissue in the peritoneal cavity, as well as vascular and lymphatic spread of viable endometrial cells to distant sites and intraoperative iatrogenic implantation - the so called metastatic theory.

This is the most accepted theory, since the existence of retrograde menstruation has already been proven by several studies and its incidence is greater among women with intense retrograde flow due to obstructive anomalies of müllerian duct development (for example, women with a unicornuate uterus with a noncommunicating rudimentary horn or uterus didelphys with a transverse vaginal septum).

2) Differentiation of pelvic peritoneal tissue into functioning endometrial cells (since both tissues share the same origin in the coelomic epithelium) - the so called metaplastic theory.
3) Release of substances by the endometrium that induce undifferentiated mesenchyme to form endometriotic tissue - the so called induction theory

development of endometriosis is currently under investigation.

A genetic basis has also been suggested, based on the high prevalence of the disease in some families.

Although the most common site of involvement by endometriosis is the ovary, all pelvic organs may be affected by implants and adhesions (such as the anterior and posterior cul-de-sac, the broad ligament, the uterosacral ligament, the uterus, the fallopian tubes, the sigmoid colon, the ureter...).

Presence of endometrial glands and stroma outside the endometrium but inside the uterine myometrium is called adenomyosis, and is probably related to the existence of abnormalities in the interface between the endometrium and the subjacent myometrium.

Endometriosis can appear in the form of noninvasive superficial peritoneal implants, scattered across the peritoneum, ovaries and uterine ligaments, whose appearance at laparoscopy depends on the degree of fibrosis, scarring, and hemorrhage within the lesion. These implants, when small sized, are frequently not detectable with magnetic resonance (MR).

It may also appear in the form of ovarian endometriomas, cystic lesions that result from invagination of superficial endometriotic lesions on the surface of the ovary and that suffer repeated cyclic internal hemorrhage during the menstrual cycle and accumulate this blood within the ovary, forming a cyst. These cysts are frequently bilateral and may be large, sometimes completely replacing normal ovarian tissue. They usually have thick and fibrotic walls and their contents, although in some cases watery, typically consist of thick and dark blood products, an appearance that has been named "chocolate cyst".

Endometrial ectopic tissue is also common within laparoscopy incisions or cesarean delivery scars, a phenomena that is thought to be independent of retrograde menstruation, probably related to direct implantation of endometrial cells during cesarean delivery or laparoscopic procedures.

Finally, endometriosis may appear in the deep/infiltrating form, defined as the migration and infiltration of endometrial tissue at least 5 mm beneath the peritoneal surface. Unlike endometriomas, which contain highly viscous proteinaceous and hemorrhagic material, these solid implants are composed of ectopic endometrial glands and stromal cells
wrapped in dense fibrous tissue and smooth muscle. Just like eutopic endometrium, these ectopic foci respond to hormonal stimulation and undergo cyclic episodes of hemorrhage, leading to a variable inflammatory reaction and subsequent fibrosis, resulting in the formation of solid nodules.

Deep pelvic endometriosis may affect several structures such as the rectovaginal septum and uterosacral ligaments, the round ligaments, the vagina, the alimentary and urinary tracts and other extraperitoneal pelvic sites, and symptoms are related to the localization of endometrial deposits and the depth of invasion.

There are no pathognomonic clinical characteristics. Symptoms of endometriosis are many times related to the response of ectopic endometrium to hormonal stimulation, resulting in cyclic hemorrhage and even in an inflammatory response that ultimately may lead to fibrosis and formation of adhesions.

The main symptoms, infertility and pelvic pain, are nonspecific, and may be present in several other disorders. To complicate things a bit further, the extent of endometriosis does not necessarily correlate with the severity of symptoms.

Nevertheless, in a woman of reproductive age with pelvic pain and/or infertility, one must strongly consider endometriosis as a possible cause.

Association between endometriosis and infertility is well established, and the most accepted causal mechanism is pelvic anatomic distortion caused by endometriomas and adhesions, which interferes with the process of ovum capture by the fallopian tubes. Autoimmune and peritoneal fluid factors have also been implied. Atypical locations of the disease (due to the presence of implants in different sites inside and outside the pelvis) may also be related to infrequent symptoms such as diarrhea, rectal bleeding and constipation (gastrointestinal involvement), urgency, frequent urination, and hematuria (bladder involvement), urinary obstruction and flank pain (ureteral involvement), pleuritic chest pain, pneumothorax, pleural effusions and cyclic hemoptysis (pulmonary involvement), headaches, seizures, and subarachnoid hemorrhage (brain involvement) and catamenial bleeding of skin lesions and tenderness (cutaneous involvement).

In most women with endometriosis, physical examination is often normal or nonspecific. Findings may include tenderness along the uterosacral ligaments and cul-de-sac, tenderness or palpable masses in the adnexal areas and fixed pelvic organs due to the presence of adhesions.
Findings and procedure details

The gold standard for the diagnosis of pelvic endometriosis is laparoscopy, which also allows staging of the disease. Histological confirmation through biopsy of suspicious lesions is preferable but not indispensable.

The main limitation to laparoscopy is the presence of adhesions that can compartmentalize the pelvis and preclude the procedure.

In terms of radiologic evaluation, ultrasonography (US), although being the first technique used to assess pelvic disease in the reproductive age group, plays a modest role in the detection and characterization of endometriotic cysts and superficial implants in surgical scars. Its accuracy in the detection of deep endometriotic lesions is operator dependant and varies according to the location of the lesions.

Rectal endoscopic US using high-frequency probes may be useful in the diagnosis of bowel wall infiltration, by detecting endometriotic foci in the rectum, rectovagina, uterosacrum and rectosigmoid region.

However, MR is the noninvasive imaging modality with the highest specificity and sensitivity for the diagnosis of endometriomas, as well as for the detection and assessment of extension of deep infiltrating disease. Superficial peritoneal implants and extraperitoneal lesions are also depicted. It allows multiplanar evaluation with high special resolution images, and it doesn’t require ionizing radiation or iodinated contrast agents.

Compared to US, MR has a larger field of view, allowing a complete survey of the anterior and posterior compartments of the pelvis, and overcomes the presence of adhesions.

It enables preoperative evaluation of disease extension and adequate surgical planning.

However, as mentioned before, none of these techniques allow screening of small, flat and nonhemorrhagic superficial peritoneal implants.

Besides, when there is clinically suspected endometriosis, normal MR does not rule out the presence of endometriosis.

**MR protocol**

A specific external pelvic coil should be used, since it delivers higher signal-to-noise, therefore improving spatial resolution and allowing acquisition of imagens with greater anatomic detail.
A 6 hour period of fastening is advisable before the exam.

Preferentially, MR should be performed with moderate bladder repletion, since an empty or overfilled bladder may conceal detection of small lesions in the adjacent recesses.

No special bowel preparation is required. However, antiperistaltic medication given before the exam decreases bowel movement, therefore reducing motion related artifacts associated with the long imaging time of MR, as well as attenuating uterine contractions.

When symptoms related to rectal involvement, such as constipation, hematochezia or painful defecation are present, endorectal gel or saline solution can be administered. In order to obtain better assessment of the retrocervical area and vaginal fornices, intravaginal aqueous gel can also be administered to distend the vaginal cavity.

MR protocol for detecting the presence and evaluating the extent of endometriosis is quite simple, based on routine T1-weighted (T1-W) and T2-weighted (T2-W) pulse sequences and on standard projections (axial, sagittal and coronal).

The sagittal plane allows excellent assessment of the cul-de-sac and rectum.

T1-weighted sequence with fat suppression is particularly important and should always be performed. On T1-W images, endometriomas have relatively homogeneous high signal intensity, similar to or even higher than that of fat. Fat suppression cancels the high signal of surrounding fat, consequently enhancing detection of the lesion. It also helps differentiating blood in endometriomas from lipid containing ovarian lesions such as dermoid cysts, as well as from fat in mature cystic teratomas, since they all have high signal intensity on T1-W images, but hemorrhage foci maintain high signal intensity after fat saturation, while fat doesn't.

Intravenous contrast administration is not necessary and brings no additional benefit in the evaluation of endometriosis, unless a malignant lesion (for example, ovarian carcinoma) needs to be ruled out. When there is a concern for malignancy, T1 and T1 fat suppressed sequences before and after gadolinium administration, as well as diffusion-weighted imaging may be added to the protocol.

In post-contrast image, it is important not to mistake normally enhancing parametrium with endometriotic foci.

Signal intensity of endometrial implants on MR depends on their contents, which mostly include proteins and degraded blood products in different proportions, according to the stage of hemorrhage.

Lesions usually have low to intermediate signal intensity on T2- and T1-W images.

Acute haemorrhage is hypointense both on T1 and T2-W images.
High signal intensity punctate foci on T2-W images may represent dilated endometrial glands.

Degraded blood products (including methemoglobin, concentrated protein and iron), which are frequent in endometriosis, usually have hyperintense signal on T1 and hypointense signal on T2-W images.

**MR features of endometriosis**

- **Endometriomas**

Endometriomas (Fig. 1, 2) are cystic masses, solitary or multiple, sometimes complex, usually having a thick and fibrous wall. They exhibit homogeneous high signal intensity on T1-W images and variable signal on T2-W images, ranging from a low to an intermediate and even to high signal intensity, according to the degree of internal hemorrhage and the concentration of blood products.

Frequently there is a loss of signal intensity on T2-W images, a phenomena named "shading", that represents cyclic and recurrent hemorrhage inside these lesions over months to years, resulting in accumulation of very viscous contents, highly concentrated in protein and iron. These high concentrations lead to protein cross-linking and consequently to a decrease in T2-relaxation time (signal loss on T2-W images). However, shading can be quite variable, ranging from a faint signal loss to complete signal void, according to the concentration of blood products.

As mentioned before, on fat saturation sequences, blood foci inside endometriomas maintain high signal intensity, allowing differentiation from fat containing lesions (dermoid cysts and mature cystic teratomas). Differential diagnosis of endometriomas also includes mucinous lesions and hemorrhagic masses. Mucinous lesions may have high signal intensity on T1-W images, but this signal is less intense than the one of fat or blood. But hemorrhagic lesions (like hemorrhagic corpus luteum, for example) may have a very similar behavior to endometriomas on MR, making it very difficult to distinguish these two entities. Hemorrhagic cysts are usually unilocular, do not show shading on T2-W images and resolve with time, whereas endometriomas are frequently multilocular and bilateral, exhibit shading on T2-W images and do not experience spontaneous resolution.

Although ovarian carcinoma may also show internal hemorrhage with high signal intensity foci on T1-W images, these lesions generally have signs of malignancy, such as solid components and septations.

Endometriomas may or may not show restricted diffusion on diffusion-weighted images, and when they do, this is perhaps because of intracystic blood clots. Enhancement after
contrast administration depends on the degree of inflammatory reaction, glandular tissue and fibrosis within the lesion.

- **Superficial endometriosis**

  Consists of superficial lesions, usually flat and small, dispersed across the peritoneum, ovaries and uterine ligament. These lesions can only be depicted by MR imaging when their size exceeds 5mm or when they have an hemorrhagic component (showing high signal intensity on T1 and low signal intensity on T2). Otherwise, they frequently pass unnoticed, for MR imaging is not sensitive enough to detect them.

- **Deep pelvic endometriosis**

  The most affected locations are the uterosacral ligaments, sometimes coexisting with infiltration of the rectal wall (Fig. 4). Very small lesions in this region may be very hard to depict on MR, but thickening of the ligaments may lead to the diagnosis. If the ligaments are thickened more than 9mm in size or if they show atypical nodularity, in a suitable clinical context, one must suspect deep infiltrating endometriosis.

  Another possible location of deep pelvic endometriosis is the round ligaments, with MR images showing T2-hypointense thickening or nodularity with enhancement after contrast administration. Curiously, the right round ligament is usually more commonly affected than the left one, probably because the presence of the sigmoid colon restricts retrograde implantation of endometrial tissue on the left side.

  The rectouterine pouch may also be affected, and endometriotic implants in this location can extend to the posterior uterus, invading the myometrium and mimicking posterior intramyometrial adenomyosis. However, unlike adenomyosis, solid rectouterine implants that involve the uterus tend to spare the uterine junctional zone.

  Implants on the vesicouterine pouch may be adherent to the anterior uterus surface, sometimes causing anteflexion of the uterus and obliteration of the anterior cul-de-sac.

  Regarding gastrointestinal tract involvement, endometriosis mainly affects the rectosigmoid colon, appendix, cecum and terminal ileum, rarely extending to more proximal segments. Endometrial cells are usually superficial and stay adherent to the serosa, although in infrequent occasions they can infiltrate the subserosa and reach the muscularis propria, causing its thickening. Only rarely implants reach the mucosa.

  Recurring hemorrhage with local inflammatory reaction may induce adhesion formation, focal strictures and even stenosis with obstruction, especially when there is circumferential wall involvement.
MR accurately evaluates the location and depth of bowel wall invasion, as well as the length of the affected area, and helps in the discrimination between an endometrial lesion and a tumor. A specific finding of solid invasive endometriosis of the rectosigmoid colon is the "mushroom cap" sign on T2-W sequences. The base of the "mushroom" has low signal intensity, reflecting hypertrophy and fibrosis of the muscularis propia, and the cap has high signal intensity, representing the mucosa and submucosa which are displaced into the bowel lumen.

Deep rectal involvement may be difficult to determine on conventional MR, due to artifacts caused by rectal contents, nevertheless, some strategies can be used in order to minimize this problem, such as the use of phased array coils, endovaginal coils and rectal contrast enema.

Regarding genitourinary tract involvement, the bladder is the most commonly involved organ, especially its posterior wall, sometimes partially or completely obliterating the vesicouterine pouch.

Dysuria is the main symptom, and cyclical hematuria, although less frequent, suggests extension of endometriosis through the detrusor muscle.

As with bowel involvement, endometrial cells often stay confined to the serosa, but in few cases they can infiltrate the bladder wall until they reach the muscle and cause wall thickening or even mural masses that project into the lumen.

MR, particularly T2-W imaging, shows localized or diffuse wall thickening, with low T2 signal intensity, eventually with high signal intensity foci of dilated ectopic endometrial glands. Hyperintense foci on T1-W images are caused by hemorrhage. After contrast administration, these lesions enhance more vividly than the normal bladder detrusor.

The urether, mainly its distal segment, may also be involved, usually because of contiguous extension from the bladder, and deep infiltration of the muscularis and lamina propria can lead to luminal narrowing, eventually with dilation and obstruction of the proximal ureter that may ultimately lead to serious impairment of renal function. MR imaging shows irregular, low T2 signal intensity nodules on the ureter wall, sometimes blurring the interface of fat between the lesion and the ureter when the implants are located superficially on the serosa.

- **Adhesions**

Adhesions are a typical and feared complication of endometriosis, resulting from phenomena of inflammation and fibrosis, and on MR they appear as T1-W and T2-W low to intermediate signal intensity stands, commonly spiculated, that make organ interfaces unclear and sometimes compartmentalize the pelvis. They can be responsible for
uterus fixation and retroversion, bowel loops angulation, ovarian displacement, fallopian tube dilation with hydrosalpinx, loculation of fluid collections in the pelvis and even hydronephrosis.

A dilated fallopian tube with high signal intensity content on T1-weighted image (hematosalpinx) is strongly suggestive of endometriosis. T2 shading effect is usually absent because dilation is secondary to endometrial deposits on the serosal surface as opposed to deposits within the tubes. There serosal implants undergo recurrent hemorrhage, leading to the development of adhesion surrounding the tubes and subsequent obstruction.

- Malignant transformation

Although cases of malignant transformation are exceptional in endometriosis (1-2.5%), this small risk should not be neglected. Most malignant neoplasms (about 75%) arise from endometriosis of the ovary, and the most frequent histological subtypes are endometrioid adenocarcinoma followed by clear cell carcinoma. Stromal sarcoma arising from stromal elements is extremely rare.

Less common locations include the rectovaginal septum, rectum and sigmoid colon.

Some studies suggest that estrogen therapy may play an important role in the development of these neoplasms.

Ovarian tumors associated with endometriosis are usually low grade and tend to manifest at an earlier stage than tumors not associated with endometriosis, and therefore tend to have a better prognosis.

Individually, an elevated CA-125 is not specific for malignancy because endometriosis itself may cause a rise in this biomarker. However, an elevated protein HE4 (human epididymal secretory protein E4) is present in ovarian cancer associated or not with endometriosis, but not in benign endometriosis.

Imaging features suggesting malignancy include size increasing lesions and enhancing mural solid components (this enhancement is better depicted in dynamic subtraction images with a gradient-echo sequence). Loss of the T2 shading effect is also more often detected in malignant than in benign endometriomas, probably owing to dilution of haemorrhagic contents by tumor secretions.
Fig. 1: 49 years old, known history of uterine fibroids, regular menstrual cycles. Complains about discomfort during menstrual periods. Routine ultrasonography showed a cystic lesion in the right ovary. MR shows a cystic lesion in the right ovary, with thin internal septa, hiperintense in T1W sequences and hypointense in T2W sequences, without fat context, presenting "shading sign." highly suggestive of endometrioma. Enlarged uterus, with multiple intramural leiomyomas.

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Fig. 2: 42 years old, Regular menstrual cycles; Recurrent pelvic pain. Routine ultrasonography revealed a cystic lesion in the right ovary. MR showed a large cystic lesion with regular contours, hyperintense on T1W sequences, with signal loss ("shading") on T2W sequences, with a fluid/fluid level due to the presence of blood, without restriction to Diffusion, highly suggestive of endometrioma.

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**Fig. 3:** 44 years old, previous caesarean delivery. Recurrent abdominal pain in the caesarean scar, more intense during menstruation. MR shows retractile, spiculated lesion, extending from the right rectus abdominis muscle to the anterior wall of the uterus, isointense with the muscle on T2W sequences and with multiple hyperintense micronodular foci (red arrow). In continuity with this area there is a nodular lesion that shapes the anterior uterine contour in the cesarean scar area, showing intense hypersignal on T1W sequences and with variable signal loss ("shading") on T2W sequences (blue arrow). It extends to the vesicouterine pouch, invading the anterior wall of the bladder (green arrow). These features represent endometriosis of the abdominal wall, in the caesarean scar, and endometriotic lesion of the anterior wall of the uterus.

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Fig. 4: 33 years old, recurrent pelvic pain. Complaints about chronic diarrhea, without significant weight loss. Previous history of ovarian endometriomas. Retractile lesion in the rectouterine pouch, contacting the posterior wall of the superior segment of the cervix and the anterior wall of the rectus, which seems to be thickened. This lesion is isointense to the miometrium on T1W images, and is hypointense on T2W images, showing moderate enhancement after intravenous contrast administration. The uterosacral ligaments are slightly thickened (red arrow). These features represent deep pelvic endometriosis of the rectouterine pouch, infiltrating the uterine torus, the superior segment of the vagina, the uterosacral ligaments and anterior wall of the rectum.

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Conclusion

Endometriosis is a common and complex chronic gynecologic disorder, that affects mainly young women of reproductive age, and whose symptoms and possible complications may have a severe impact in affected patients.

Laparoscopy remains the gold standard for diagnosis of pelvic endometriosis, however this procedure has some limitations regarding detection of lesions in the subperitoneal space, and is conditioned by the presence of adhesions that may impede visualization of lesions deeply located in the pelvis.

MR is the noninvasive method with highest diagnostic accuracy for endometriosis, which allows depiction of several forms of manifestation of this disorder, including endometriomas, superficial and deep pelvic endometriosis, therefore enabling a more accurate evaluation of disease extension.

Combining information regarding the possible locations and typical clinical features of endometriosis helps radiologists to better understand radiologic appearances of the disease and to suggest this diagnosis more accurately.
References