MR imaging of endometriosis: Spectrum of disease

C. Bourgioti a, *, O. Preza a, E. Panourgias a, K. Chatoupis a, A. Antoniou a, M.E. Nikolaidou b, L.A. Moulopoulos a

a Department of Radiology, School of Medicine, National and Kapodistrian University of Athens, Aretaieion hospital, 76, Vassilisis-Sofias Ave., 11528 Athens, Greece
b Department of Gynaecology and Obstetrics, Rea maternity hospital, 383, Sygrou Ave., 17564 Athens, Greece

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Abstract Endometriosis is a common gynecological disorder defined by the presence of endometrial tissue outside the uterus. It is the most common cause of chronic pelvic pain and typically affects the ovaries, uterine ligaments, peritoneum, tubes, rectovaginal septum and bladder. It may, however, be found at various extrapelvic sites, including the perineum, liver, pancreas, lung or even the central nervous system, and in such cases, diagnosis may be quite challenging. Even though definitive diagnosis requires laparoscopy, preoperative identification of endometriosis is important not only to differentiate it from other diseases with similar clinical presentations but also, for accurate presurgical mapping, since complete removal of all endometriotic foci is critical for the effective treatment of the patient’s symptoms. Ultrasound is performed initially, but magnetic resonance imaging (MRI) is increasingly being used, particularly when sonographic findings are unclear, when deep pelvic endometriosis is suspected or when surgery is planned, as it provides better contrast resolution and a larger field of view compared to ultrasound. In this article, we will discuss distinctive MRI appearances of endometriotic foci and we will review common and uncommon locations of endometriosis within the body, in an attempt to familiarize radiologists with its wide spectrum of manifestations.

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* Corresponding author.
E-mail addresses: charisbourgioti@yahoo.com (C. Bourgioti), prezarania10@gmail.com (O. Preza), epanourgias@yahoo.com (E. Panourgias), kchatoupis@yahoo.gr (K. Chatoupis), aantoniou@med.uoa.gr (A. Antoniou), marilianikolaidou@gmail.com (M.E. Nikolaidou), lmoulop@med.uoa.gr (L.A. Moulopoulos).

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Endometriosis is a common gynecological disorder defined by the presence of endometrial tissue outside the uterus. It is the most common cause of chronic pelvic pain and typically affects the ovaries, uterine ligaments, peritoneum, tubes, rectovaginal septum and bladder. It may, however, be found at various extrapelvic sites, including the perineum, liver, pancreas, lung or even the central nervous system, and in such cases, diagnosis may be quite challenging. Even though definitive diagnosis requires laparoscopy, its preoperative identification of endometriosis is important not only to differentiate it from other diseases with similar clinical presentations, but also for accurate presurgical mapping, since complete removal of all endometriotic foci is critical for the effective treatment of symptoms. Ultrasound is performed initially, but magnetic resonance imaging (MRI) is increasingly being used, particularly when sonographic findings are unclear, when deep pelvic endometriosis is suspected or when surgery is planned, as it provides better contrast resolution and a larger field of view compared to ultrasound.

In this article, we will discuss distinctive MRI appearances of endometriotic foci and we will review common and uncommon locations of endometriosis within the body, in an attempt to familiarize radiologists with its wide spectrum of manifestations.

General principles

Incidence, location, types and clinical presentation of endometriosis

Endometriosis affects up to 10% of women at childbearing age [1,2]. Only 5% of cases involve the postmenopausal population and these are most often in association with exogenous estrogen replacement. Endometriosis can be either intra- (much more frequently) or extrapelvic in location. Intrapelvic ectopic endometrial glands and stroma are most often in the ovaries but may also involve the uterosacral ligaments and cul-de-sac, serosal surfaces, fallopian tubes, rectosigmoid colon, vagina, cervix, bladder and ureters. Extrapelvic endometriosis is much less frequent, occurring in about 1% of all cases, and may be seen at virtually any anatomic location, including the abdominal wall, surgical scars, diaphragm, liver, kidneys, pancreas or even bones and brain [3].

There are three types of endometriosis. In superficial endometriosis, endometriotic foci (usually very small and identifiable only at laparoscopy) are located at the peritoneal surface or less than 5 mm from it. In deep (or solid infiltrating) endometriosis, endometrial implants are located at least 5 mm away from the peritoneal surface and may invade the retroperitoneal space or the wall of adjacent pelvic organs. Symptomatic patients usually suffer from deep endometriosis. Finally, endometriomas, the third type of endometriosis, present as cystic structures with hemorrhagic content located at the adnexa.

Common clinical manifestations, include pelvic pain (cyclical pelvic pain, dysmenorrhea and dyspareunia) and infertility. Deep endometriosis is considered the main cause of chronic pelvic pain in women of reproductive age. Less frequent symptoms, such as: painful constipation, catamenial diarrhea, rectal bleeding, hematuria or rarely, pneumothorax or epistaxis are closely related to the location of the ectopic, functional endometrium; interestingly, a number of patients may be asymptomatic.

Pathogenesis

The etiology of endometriosis is even today under investigation. The most popular theory for its pathogenesis is that of retrograde menstruation, where endometrial cells migrate through the fallopian tubes to the peritoneum during menstruation, and there they grow, under the influence of hormonal and other factors (Sampson’s theory). Coelomic metaplasia (cells of the coelomic epithelium which covers the ovaries and the peritoneum transform to endometrial cells), or growth of ectopic primitive cells outside the Mullerian tracts, have also been implicated as possible causes of endometriosis. More recently, other theories such as transformation of circulating stem cells into endometrial tissue are being considered as well [4].

Diagnosis

Laparoscopy is the gold standard for the diagnosis of endometriosis [5]. Sometimes, surgical exploration can be complicated, as deep endometriotic plaques may be hidden under extensive adhesions or may not be visible due to a subperitoneal location. One-step surgery (i.e., diagnosis and complete excision of the lesions at the same time) is essential for the successful treatment of endometriosis and, therefore, presurgical mapping of the endometriotic lesions becomes an important issue [5]. Currently, ultrasound is preferred for the initial assessment of both endometriomas and deep pelvic endometriosis. However, transvaginal ultrasound, even with adequate bowel preparation and use of high-frequency probes has important limitations, because of the relatively small field-of-view and operator dependency [6]. MRI is being increasingly used for the evaluation of endometriosis, with reported sensitivity and specificity values ranging from 69–92% and 75–98%, respectively [7–9]. Most authors advocate MRI as an adjunct tool in cases of ultrasound-indeterminate findings, possible ureteral involvement and presurgical mapping [6].

MRI protocol

Recently, the European Society of Urogenital Radiology (ESUR) published specific guidelines focusing on patient preparation, optimal MRI sequences and reporting criteria for the evaluation of patients with endometriosis [6].

Fasting (at least 4–6 h prior to the examination) and administration of antiperistaltic agents (intramuscularly or intravenously) is strongly recommended for better image quality. The bladder should be moderately filled; vaginal and/or rectal opacification is optional. The majority of MRI studies are performed at high field magnets (1.5 T or 3 T) with the use of pelvic phased array coils. T2-weighted sequences are most suitable for demonstrating pelvic endometriosis; T1-weighted images with and without fat suppression are helpful for depicting ovarian endometriomas. Fat-suppressed, T1-weighted images appear to be
of value for the detection of peritoneal lesions, but data are still under investigation [10,11]. The use of intravenous gadolinium chelate is not mandatory for the evaluation of deep pelvic endometriosis. However, MRI with the adjunct of intravenous administration of gadolinium chelate may provide useful information in cases of atypical adnexal lesions (e.g. cysts with mural nodules). Current data do not support the role of diffusion-weighted imaging (DWI) or susceptibility weighted (SW) images. The MRI protocol applied at our institution is presented in Table 1.

MRI features of endometriotic foci with histopathologic correlation

MRI findings of endometriosis are closely related to the histology of the disease. Since endometriotic foci consist of functional endometrium, they respond to hormonal stimulation during the menstrual cycle as normal endometrium does. Ectopic endometrial glands may appear as foci of variable signal intensity on T2- and T1-weighted images, depending on the age of hemorrhage. Subacute bleeding may result in very high signal intensity on T1-weighted images, which is usually more conspicuous on images with fat suppression, and relatively low signal intensity on T2-weighted images.

In women with chronic endometriosis, recurrent bleeding of the ectopic endometrium induces the development of reactive fibrosis. These fibrotic endometrial lesions, present with an irregular spiculated contour and relatively low signal intensity on both T1- and T2-weighted images. Careful search for small foci of high signal intensity on T2-weighted and often high signal intensity on T1-weighted images, related to the presence of dilated endometrial glands within the fibrotic tissue, enables the diagnosis since the low signal intensity on T2-weighted images of these lesions is similar to that of the wall of normal pelvic organs. Foci of chronic endometriosis show variable enhancement on MR images obtained after intravenous administration of gadolinium chelate.

Adhesions, in cases of long-standing endometriosis, may be seen, as low signal intensity bands on T2-weighted images of variable thickness, extending between pelvic organs. Sometimes, they may be too thin to be visualized on MRI; indirect signs, such as distorted anatomy (e.g. uterine retraction), dilated tubes, peritoneal inclusion cysts or bowel angulation may suggest the presence of pelvic adhesions [4].

Distribution of endometriosis

Frequent sites of endometriosis

Endometriomas

The adnexa is the most common location of endometriosis. Endometriotic cysts (or endometriomas) are localized forms of ovarian endometriosis; they can be solitary or multiple, unilateral or, in almost 50% of women with endometriosis, bilateral. MRI has high specificity (>90%) in identifying endometriomas. They are thick wall cysts with blood products related to cyclic bleeding. That is why, endometriomas, typically, present with bright signal intensity on T1-weighted images (T1 shortening is due to the presence of subacute hemorrhage and high protein content) and homogeneously low signal intensity on T2-weighted images (T2 shading—caused by accumulation of iron and protein due to repeated bleeding) [12,13]. T2 shading has high sensitivity (93%) but poor specificity (45%) for the diagnosis of endometriomas, and it may occasionally be seen in other hemorrhagic adnexal lesions. In such cases, it may be helpful to look for the T2 dark spot sign which consists of small- usually multiple- foci of very low signal intensity on T2-weighted images within the cyst but not in its wall (Fig. 1). These dark foci on T2-weighted images are highly indicative of long standing hemorrhage (they possibly represent chronic retracted clots) and may, therefore, they may be helpful in discriminating endometriomas from other functional hemorrhagic lesions [14]. Another distinctive MR

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which intensity intensity (acute component obtained the appearing therefore, also the administration nomonic) malignancy, chelate also the endometriomas of cysts appearing on axial plane, showing bilateral endometriomas with multiple small foci of very low signal intensity within the cysts (arrows). These dark foci on T2-weighted MR image are highly indicative of repeated bleeding and possibly represent chronic retracted clots (dark spot sign).

Figure 1. 32-year-old woman with known history of endometriosis. T2-weighted MR image in the axial plane shows bilateral endometriomas with multiple small foci of very low signal intensity within the cysts (arrows). These dark foci on T2-weighted MR image are highly indicative of repeated bleeding and possibly represent chronic retracted clots (dark spot sign).

Feature of endometrioma is the presence of a low signal intensity peripheral rim on T2-weighted images, caused by hemosiderin-laden macrophages within the wall of the lesion; fluid-fluid levels, due to recent bleeding, may also be seen on T2-weighted images, with the low signal intensity of the dependent portion caused by the cellular component of bleeding [4].

The differential diagnosis includes hemorrhagic cysts (acute presentation, lack of T2 dark spot sign, resolution in 4–6 weeks), teratomas (the presence of fat is pathognomonic) and ovarian carcinoma (usually solid elements, which enhance on MR images obtained after intravenous administration of gadolinium chelate). Note that a solid-appearing wall nodule, a suspicious finding for ovarian malignancy, may also be found in a considerable number of endometriomas (20%). However, in endometriomas, the nodule possibly corresponds to a retracted clot, and, therefore, does not usually show any uptake on MR images obtained after intravenous administration of gadolinium chelate [4]. Multiple bilateral endometriomas (50%) with coexisting adhesions cause retraction of the ovaries which come to abut each other, the so-called kissing ovaries (Figs. 2 and 3).

Rarely, large endometriotic cysts (maximal diameter > 6 cm) may rupture into the peritoneal cavity causing acute abdominal pain and inducing the accumulation of ascites due to peritoneal irritation from blood products (chemical peritonitis) (Fig. 4). Differential diagnosis between rupture of an endometriotic cyst versus any other ovarian haemorrhagic lesion (e.g. a corpus luteum cyst—which is far more common) may be difficult and often laparoscopy is needed to identify the source of bleeding; bilateral hemorrhagic lesions, lobulated ascites (due to presence of adhesions) confined to the pelvis and high serum CA-125 levels, are common findings in women with a ruptured endometriotic cyst [15,16].

Infected endometrioma is also rare, even though it is suggested that women with advanced endometriotic disease are at higher risk for developing an ovarian abscess than those without endometriosis [17]. Possible causes for

Figure 2. 39-year-old woman with long standing endometriosis. T2-weighted MR image in the axial plane demonstrates both ovaries on the right side of the pelvis, abutting each other (kissing ovaries). Also shown is a large endometriotic plaque involving the left round ligament and uterine horn (arrow), RO: right ovary, LO: left ovary.

Figure 3. 34-year-old woman with chronic pelvic pain. A. T2-weighted MR image in the axial plane clearly depicts a thick, low signal intensity band extending from the posterior uterine wall to the bowel, consistent with an adhesion (white arrow). Bilateral endometriomas and retraction of the ovaries (asterisks) to the midline due to co-existing adhesions is also shown (kissing ovaries). B. Laparoscopic image of another woman with advanced pelvic endometriosis shows the presence of adhesions (white arrow) between the posterior uterine wall (U) and the epiploic appendages (A) of the sigmoid (S). Note the endometrioma (E) of the displaced right ovary.
the dissemination of pathogens (typically polybacterial) to the ovarian endometriomas includes: transvaginal aspiration for in vitro fertilization (IVF), pelvic surgery, ascending genital tract infection, haematogeneous or even contiguous spread from adjacent organ inflammation; rarely, infection may develop spontaneously in a pre-existing endometrioma [18,19]. Imaging findings include the presence of a complex cystic adnexal mass, but, as there are only a few cases described in the literature, there are no typical MRI features for infected endometriomas. Diagnosis is based on clinical evidence and in most cases and surgical drainage is needed to optimize treatment [20].

Most of the endometriotic cysts decrease in size during pregnancy, and this is mainly attributed to high progesterone levels and temporary interruption of the menstrual cycle. However, 12% of ovarian endometriomas may undergo decidualisation (i.e. morphological and functional changes of endometrial stromal cells, which result in formation of desidua, an important structure which supports placentation) during pregnancy. MRI features of decidualized endometriomas includes the presence of solid components, papillary projections and internal septa, quite like borderline tumors or even ovarian cancer. However, it is reported that the mural nodules of the decidualized endometriomas are smaller compared to those of ovarian carcinomas. They follow the signal intensity (SI) of normal endometrial decidua/placenta demonstrating higher signal intensity on T2-weighted images, significantly higher apparent diffusion coefficient (ADC) values and absence of increased signal on diffusion-weighted images with b values of 1500 s/mm², compared to the solid components of ovarian carcinomas [21,22]. Most of the decidualized endometriomas are surgically removed because they resemble ovarian malignancies, even though several authors advocate expectance management, as desidualized endometriomas tend to regress rapidly during follow-up studies, unlike ovarian neoplasms [23].

**Uterine ligaments**

The uterosacral ligaments (USL) are major supportive uterine ligaments, which originate horizontally (distal portion) from the posterolateral aspect of the cervix (torus uterinum) or the upper vaginal dome (cervico-vaginal junction), descend in front of the anterior and lateral part of the rectum (median portion), where they are closely attached to the mesorectal fascia (i.e. the visceral layer of the endopelvic fascia which encircles the rectum and the mesorectal fat) and then course posteriorly, finally inserting into the sacrum [24], piriformis muscles or sacrospinous ligament/coccygeus muscles (proximal portion) [25]. Normally, USLs are visualized as thin, low signal intensity bands of connective tissue on MRI (Fig. 5); thin section (3 mm) oblique transverse T2-weighted MR images (oriented along the course of USLs when visible on sagittal plane or perpendicular to the long axis of the cervix, when USLs are not visible) are recommended for the demonstration of the entire course of the USLs, because of their characteristic anatomical orientation [26].

Uterosacral ligament involvement should always be looked for when endometriosis is suspected, as it is the most common location of deep endometriosis with a reported incidence up to 69.2% [27]. Associated clinical symptoms include pelvic pain and dyspareunia. It may present as asymmetrical (diffuse or focal) ligament thickening (unilateral or bilateral), or even as a nodular mass abutting the ligament. It is more frequent at the horizontal part of the ligament (close to the cervix) and spread to the extraperitoneal retrocervical region and from there to the rectum and vagina may occur. In such cases, retroversion of the uterus or rectal angulation may be observed as well (Figs. 6–8). According to several studies [28,29], radiologists may accurately identify the abnormal uterosacral ligaments, with reported uncertainty values as low as 13.8% [29].

The round ligaments are easily detected as thin low signal structures, coursing from the uterine horns anteriorly to the inguinal canal, and finally attaching to the labia majora. When involved (reported frequency rates range from 0.3% to 14%), they appear thicker (Fig. 9) and show enhancement, particularly well seen on MR images with fat-suppression obtained after intravenous administration of gadolinium chelate [27,30]. This information may be helpful to the surgeons since exploration of the round ligaments during laparoscopic surgery for endometriosis is often
be overlooked. In case of shortening, thickening or deviation, the round ligaments should be removed [31]. Women with round ligament involvement may present with a painful inguinal mass, if the inguinal segment of the ligament is involved. In such cases, differential diagnosis include more common pathologies of the groin including lymphadenopathy, hernias or soft tissue tumors which in most cases may be readily accessed by imaging.

Pouch of Douglas
Endometriosis may frequently involve the rectovaginal pouch (commonly known as pouch of Douglas); usually, MRI may demonstrate ill-defined, solid, hypointense lesions on T2-weighted images, abutting the posterior aspect of the uterine body and cervix. In some cases, MRI may show a considerable amount of glandular tissue and discrete fibrotic reaction, with variable enhancement on MR images obtained after intravenous administration of gadolinium chelate; identification of endometriotic glands as tiny foci of high signal intensity on T1- and T2-weighted images (representing subacute hemorrhage and/or high viscosity fluid) helps establish the correct diagnosis. Retrocervical lesions may extend to the anterior rectal wall, causing complete or partial obliteration of the pouch of Douglas [32]. Obliteration of the cul-de-sac may hide areas of endometriosis on laparoscopy and, thus, the extend of the disease may be underestimated during surgery [33]; preoperative MRI may be quite useful for identifying endometrial implants localized in the obliterated pouch of Douglas, with reported sensitivity and specificity values up to 89% and 94%, respectively [34].

External adenomyosis
Sometimes, deep endometriotic plaques may occur at the uterine surface and from there they may invade the myometrium mimicking adenomyosis (so-called external adenomyosis) or even subserosal leiomyomas [32]. Adenomyosis (i.e. ectopic endometrial glands within the

Figure 5. 28-year-old woman, healthy volunteer. A. Thin (3 mm) section T2-weighted MR image in the axial oblique plane demonstrates the horizontal (distal) portion of the normal, thin USLs extending from the region of cervico-vaginal junction (white arrows). B. Corresponding T2-weighted MR image in the sagittal plane shows the normal horizontal aspect of the left USL (arrow). USLs descend in front of the anterior and lateral part of the rectum (median portion) and finally insert into the sacrum or the adjacent muscles (proximal portion).

Figure 6. 30-year-old woman with endometriosis and a history of chronic pelvic pain and dyspareunia. A. T2-weighted MR image in the axial plane shows asymmetrical thickening of the right uterosacral ligament (arrow), a common site for endometriosis. B. T2-weighted MR image in the coronal plane shows uterine angulation (white arrow), due the presence of adhesions. An incidental ovarian cyst is seen on the left (asterisk).
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**Figure 7.** 43-year-old woman with deep infiltrating endometriosis. A. T2-weighted MR image in the axial plane demonstrates a typical endometriotic plaque at the distal portion of the right uterosacral ligament (USL - long white arrow). Note the endometriotic implants within the paracervical space bilaterally (short white arrows). B. Corresponding T2-weighted MR image in the sagittal plane clearly depicts the entire course of the right USL (white arrow points to the lesion, black to the normal portion of the ligament). C. Laporoscopy confirmed the presence of USL endometriosis (white arrow). Black arrows point to the unaffected part of the right USL.

**Figure 8.** 39-year-old woman with chronic pelvic pain. A. T2-weighted MR image in the axial plane and corresponding laparoscopy image. B. Show a retractile endometriotic lesion at the torus uterinum (long arrows). Note the normal round ligament on the left (small arrows). U: uterus, O: ovary.

Myometrium) is a common finding in patients with endometriosis, therefore, discrimination between the two entities may be difficult, although necessary due to differences in treatment [35]. Extension of the lesion beyond the uterine contour, continuity with an adjacent endometriotic plaque and visualization of an intact transitional zone favor endometriosis over adenomyosis (Fig. 10). Indistinct margins and high signal intensity foci on T1-weighted images within the lesion favor endometriosis over leiomyomas [32].

**Fallopian tubes**

Almost 30% of women with endometriosis present with fallopian tube involvement at laparoscopy. Ectopic

**Figure 9.** 43-year-old woman with known history of endometriosis. A. T2-weighted MR image in the axial plane shows an abnormally thickened left round ligament (black arrow). B. Laparoscopic image shows a thick round ligament on the left (small arrows) and multiple small endometriotic foci on its surface. A dilated left fallopian tube is also demonstrated (FT). U: uterus, O: ovary.
endometriotic implants in its wall [36]. Hydrosalpinges may also occur with pelvic endometriosis, due to chronic adhesions. However, remember that the most frequent cause of hydrosalpinx is pelvic inflammatory disease and not endometriosis [12,20].

Gastrointestinal endometriosis

The gastrointestinal tract (GI) is the most common site of extragenital endometriosis and it is frequently involved in women with deep invasive endometriosis. The rectosigmoid colon is the most frequently encountered site of GI endometriosis, followed by the sigmoid colon, with a reported incidence up to 65.7% and 19%, respectively. Endometriotic lesions may be multifocal in more than half of all cases with rectal involvement [37]. The ileum, cecum and appendix are other, less frequently involved GI locations, with a reported incidence ranging between 1% and 7% in women with bowel endometriosis; in rare cases, the ileocecal region may be the only site involved [38]. Interestingly, in approximately 30% of cases with rectal and sigmoid involvement, right-sided bowel endometriosis is also present [37]. Furthermore, recent reports addressed a possible association between ileocecal/appendix endometriosis and right ureteral involvement [39]. Therefore, in women with deep invasive endometriosis the bowel proximal to the rectosigmoid junction should also be carefully examined.

Endometriotic bowel implants are usually located at the serosal surface, but transmural involvement may occur. Typical MRI findings of deep rectosigmoid endometriosis include a lesion of low signal intensity on T2-weighted images at the bowel wall (induced fibrosis and hypertrophy of the muscularis propria), with a high signal intensity shell projecting into the bowel lumen (protruding mucosa and submucosa); this is the so-called “mushroom cup” sign of endometriosis of the bowel (Fig. 12) [12,20,30,32]. MRI may be useful to demonstrate the involvement of the muscle layer of the bowel wall by endometriotic implants, but it has limitations in assessing true submucosa/mucosa infiltration, which requires more radical surgical treatment [40].

Usually, ileal endometriosis affects the terminal ileum, within an approximately 10 cm distance from the ileocecal valve. However, concurrent lesions may occur at more proximal small bowel loops [37]. Imaging findings include the presence of fibrotic nodular or retracile masses of low signal intensity on T2-weighted images with or without high signal hemorrhagic foci on T1-weighted images with fat suppression, abutting the bowel wall (Fig. 13). Although it is reported that preoperative imaging is usually inadequate to demonstrate ileal involvement and commonly the diagnosis of ileal endometriosis is made during surgical exploration for colorectal endometriosis [38], in the study conducted by Rouset et al., 3.0-T MR enterography exhibited excellent diagnostic performance for the diagnosis and mapping of endometriotic lesions located at the ileocecal region, with 100% positive predictive value [37].

Preoperative work-up for the localization of bowel endometriosis is necessary for optimal therapeutic management. Surgical treatment of deep invasive endometriosis, especially when the rectosigmoid is involved, may be associated with complications such as rectovaginal fistula, pelvic abscess formation or anastomotic leak in cases of segmental
bowel resection [39]; it is, therefore, suggested that the "least radical option should be selected" [41]. MRI may help surgeons plan more conservative surgical approaches in case of rectal and/or sigmoid involvement like rectal shaving, mucosal thinning or full-thickness anterior rectal wall excision (also known as disc resection); lack of multifocal disease, small size lesions (maximal diameter < 25–30 mm), absence of submucosa/mucosa infiltration, low (less than one third) percentage of intestinal circumference affected by the disease and sufficient distance (> 10 cm) between the rectal endometriotic implant and the anal verge are considered important for the selection of candidates for less radical bowel surgery [40].

Parametrial involvement
Deep pelvic endometriosis may also affect the parametrial space; the prevalence of parametrial involvement is estimated up to 14.5% of cases with deep infiltrating disease [42]. Preoperative MRI may show irregular low signal intensity lesions with or without bright foci on T2-weighted images in the paracervical or paravaginal region (Fig. 7); in case of severe endometriosis, pelvic side wall involvement may be seen on MR images, usually as a mass like fibrotic tissue occupying the parametrial space and extending to the pelvic muscles. Ureteral dilatation is considered an indirect sign of parametrial involvement [42]. Identification of endometrial implants within the parametrial fat is important for surgical planning; in cases with parametrial involvement, parametrectomy may be required for the complete excision of deep endometriosis. This procedure is technically challenging and may be complicated with either ureteral injury or secondary urinary or large bowel dysfunction, due to nerve trauma [43].

Bladder
Urinary tract involvement occurs in almost 4% of patients with endometriosis. The posterior bladder wall is most frequent affected (90%). In 50% of patients with bladder endometriosis, there is a history of prior C-section or other gynecologic surgery [12,13]. Women present with dysuria and less often hematuria indicating involvement of the bladder mucosa. MRI demonstrates sensitivity and specificity values equal to 68% and 98%, respectively, for identifying bladder involvement in patients with deep endometriosis [34] and may show endometriotic lesions even in patients with normal cystoscopic findings or with no urinary tract symptoms. Bladder endometriosis appears as a low signal intensity nodule on T2-weighted images with small bright foci at the posterior bladder wall possibly extending to the vesicouterine pouch (Fig. 14) [12,44].

Figure 12. 36-year-old woman with history of endometriosis and painful defecation. T2-weighted MR image in the sagittal plane shows endometriotic implant invading both the posterior uterine and the anterior sigmoid wall. The lesion protrudes into the colonic lumen creating the mushroom cap sign with the bright peripheral signal representing the colonic mucosa (white arrow) which surrounds the low signal endometriotic lesion (asterisk).

Figure 13. 45-year-old woman with abdominal pain and vomiting. A. T2-weighted MR image in the coronal plane shows a low signal intensity mass-like lesion on the right side of the lesser pelvis (asterisk), inseparable from dilated terminal ileum loops (white arrows in A and B). B. Corresponding T2-weighted MR image in the sagittal plane demonstrates the relation of the mass (asterisk) with the adjacent cecum (C). A large endometriotic lesion invading terminal ileum was found at laparoscopy.
Ureteral involvement may be present even with minimal disease, in patients with extensive deep infiltrating pelvic endometriosis [45]; in rare cases, isolated ureteral endometriosis may be found in the pelvis, resembling a ureteral tumor. That is why endometriosis should be included in the differential diagnosis of non-calculus ureteric obstruction or/and ureteric intraluminal lesions in young women [46]. Endometriotic plaques with low signal on T2-weighted images with or without bright signal foci, adhesions and ureteral dilatation proximal to the site of obstruction are MRI common findings (Fig. 15). Identification of ureteral endometriosis is important because advanced surgical techniques, like ureter diversion or reimplantation are often required [32].

Figure 14. 40-year-old woman with history of endometriosis and dysuria. T2-weighted MR image in the sagittal plane shows a low signal intensity lesion disrupting the posterior wall of the bladder (arrow). Note the multiple tiny high signal foci within the lesion, representative of the dilated ectopic endometrial glands.

Less frequent sites of endometriosis

Abdominal wall

The abdominal wall is the most common location of extra-abdominopelvic endometriosis. It is often associated with prior laparoscopic or surgical intervention and, in most cases, there is no history of prior endometriosis. It is estimated that almost 0.03–0.4% of women with a prior C-section and 1.08–2% with prior hysterotomy, will develop endometrial implants at the surgical scar [47]; it is most frequently seen a year after surgery. Common locations include the abdominal subcutaneous tissue and less often the rectus abdominis muscle and its sheath as well as the region of the umbilicus. Clinical symptoms include a constant, atypical localized pain with or without a palpable mass, which can be frequently misdiagnosed [20,47]. MRI is used to define the extent of the disease and to evaluate the imaging characteristics of the lesion (Fig. 16). Fine needle aspiration is often required for the diagnosis. Differential diagnosis includes a desmoid tumor, which may present with very low signal intensity on T2-weighted images due to fibrin deposition without, however, the bright signal on T2-weighted images of the dilated endometrial glands [12], hematoma, sarcoma, lymphoma and primary or metastatic cancer.

Vagina and vaginal vault

Vaginal endometriosis is usually associated with perineal scar endometriosis, which is an unusual entity (0.3—1% of women) occurring at the episiotomy scar after prior vaginal delivery. Secondary vaginal vault endometriosis has also been described in women with bilateral oophorectomy.
and hysterectomy due to vaginal-uterine morcellation [32,48,49]. Thickening and loss of the low signal intensity of the posterior vaginal wall on T2-weighted images, are common findings; hemorrhagic nodules and/or ill-defined fibrous masses with or without high signal foci on T2-weighted images may also be seen (Fig. 17) [50].

**Abdominal viscera**

Endometriosis is extremely rare outside the pelvis although it has been reported to affect almost every organ, with the exception of the heart and spleen. Liver endometriosis is a rare entity with less than 30 cases described in the literature, half of which had no previous history of endometriosis [51,52]. It is likely that, some cases of liver endometriosis probably arose from an extracapsular location and then invaded the parenchyma; in such cases, patients may present with right upper quadrant abdominal pain. Liver endometriomas may be imaged as complex masses, with variable amounts of solid and cystic/haemorrhagic components (Fig. 18). Differential diagnosis of liver endometriomas may be challenging and includes primary hepatic tumors (e.g. adenoma), echinococcal cysts, metastases or mucinous neoplasms, which may also demonstrate high signal on T1-weighted images. Intraoperative frozen section biopsy is needed to establish the diagnosis.

Pancreatic endometriosis is very rare, with less than 10 cases reported in the medical literature. Clinical presentation or imaging findings are non specific [53]; differential diagnosis includes other pancreatic tumors, such as mucinous cystic neoplasm or pseudocyst and, therefore, surgical exploration is often required for a definitive diagnosis.

**Thoracic endometriosis**

The thorax is the most frequent extra-abdominal site of endometriosis; however, it is rarely involved. Ectopic endometrial tissue may be found in several thoracic structures including the pleura, lung parenchyma, pericardium or the diaphragm, resulting in a wide spectrum of clinical and radiological manifestations which follow the cyclic endometrial changes, the so-called thoracic endometriosis syndrome [54]. Catamenial pneumothorax is the most common clinical presentation; periodical hemotherax, hemoptysis, chest or scapular pain or even lung nodules are other manifestations. Radiological features are non-specific; therefore, for most authors, imaging has a limited role in the diagnosis of thoracic endometriosis [55]; it is the association of the symptoms with the menstrual circle which, usually points out the correct diagnosis [56], and thoracoscopy is usually needed to confirm the clinical suspicion.

A possible explanation for the thoracic involvement suggests that the ectopic endometrium follows a circle “route” (along with peritoneal fluid) within the abdomen and via the right paraocolic gutter may be implanted to the peritoneal surface of the diaphragm; then, endometrial cells through diaphragmatic defects (congenital or
acquired) may be implanted within the thoracic cavity [57,58]. This phenomenon explains the increased frequency of right cataminal pneumothorax [54]. According to another theory (microembolization theory), endometrial cells are implanted in the pulmonary parenchyma via a pulmonary network filter function, forming well circumscribed nodules (solitary or multiple) which are usually located at the peripheral bronchi or, less frequently, within the lung parenchyma. This theory possibly explains the clinical symptom of haemoptysis, as well as the bilateral or left-sided location (30%) of lung nodules [54].

MRI may demonstrate small hyperintense on T1-weighted images endometriotic lesions in the visceral or parietal pleura [54]. Diaphragmatic endometrial implants may be identified as hyperintense foci on all MRI sequences, almost always involving the right hemidiaphragm, and particularly its posterioperior surface. Although the small size of the lesions and susceptibility artefacts may limit the diagnostic performance of MRI in cases of thoracic endometriosis, Rousset et al. reported high (> 80%) MRI sensitivity and excellent interobserver agreement in detecting diaphragmatic endometriosis in symptomatic patients [59]. MRI may therefore allow early identification of endometriotic implants in patients with diaphragmatic involvement and may help surgeons to plan the surgical removal of the lesions.

Central nervous system

Central nervous system (CNS) endometriosis is extremely rare. Only one case of cerebellar and two of cerebral endometriosis have been reported, one of the latter related to the presence of a ventriculoperitoneal shunt [60]. Patients' symptoms included headache, seizures or even subarachnoid hemorrhage; in all three cases, MRI showed a cystic brain lesion with a hemorrhagic level. Final diagnosis was based on histopathological examination. Cases of endometriosis involving the spinal canal, dura, spinal cord and vertebrae have been reported; spinal involvement is associated with periodical low back pain in women of reproductive age [61]. In all cases, only biopsy provides a definitive diagnosis.

Ischiorectal fossa

There are only few cases of endometriosis of the ischiorectal fossa in the literature [62], usually originating from an episiotomy incision [50]. In a single report by Ramalingappa et al., ischiorectal fossa endometriosis was described in a woman with uterine outflow obstruction. The authors suggested that due to increased intrauterine pressure, the menstrual blood might have dripped through the pelvic floor into the ischiorectal fossa [62]; however, this hypothesis is questionable.

MRI features includes the presence of an ill-defined lesion with hemorrhagic foci or a hemorrhagic nodule within the adipose tissue of the ischiorectal fossa. Differential diagnosis may include a tailgut cyst, which arises from the retrorectal space and may sometimes extend in the ischiorectal fossa [50].

Sciatic nerve

The sciatic nerve is a very rare site of endometriosis, with the mechanism of involvement still under debate. The right sided predominance of sciatic nerve endometriosis may be explained by the anatomic location of the sigmoid colon preventing the reflux of cells into the openings of peritoneal outpouchings towards the region of the sciatic notch or actually inhibiting these peritoneal “pockets” from reaching the notch. Coelomic metaplasia and embryonic cell rest theories have also been considered as possible mechanisms
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for endometriosis of the sciatic nerve. [63–65]. Sciatic nerve is the commonest nerve prone to endometriosis (39%), after the nerves of the lumbosacral plexus (57%), which may be affected by direct extension from adjacent endometriotic plaques. Interestingly, perineural spread of endometriosis (i.e. from an adenomyotic uterus to the lumbosacral plexus via pelvic autonomic nerves, and then distally to the sciatic nerve or even proximally to the spinal nerves) has been proposed as an alternative explanation for lumbosacral or sciatic nerve involvement, particularly in the absence of peritoneal disease [66,67]. Progressive cyclic sciatica and a hyperintense mass on T1-weighted images at the region of the lumbosacral plexus or sciatic nerve may suggest the diagnosis; nerve enlargement along with heterogeneous enhancement on MR images obtained after intravenous administration of gadolinium chelate may, also, be demonstrated [67–69]. Current data support the important role of preoperative three-dimensional (3D) MR neurography for evaluating the relationship of the sacral nerve plexus and ectopic endometrial lesions assisting potentially treatment management [70].

Nodal involvement

Although lymph node infiltration in deep endometriosis is considered to be an atypical finding, some studies suggest that nodal involvement in endometriosis might be just underestimated because most of the surgeons do not routinely perform lymphadenectomy in cases of deep infiltrating endometriosis, as the latter is considered a benign disease. In a study conducted by Noël et al., lymph node involvement was detected in up to 42.3% of 26 patients with rectosigmoid endometriosis [71]. Nodal endometriosis may be the result of extension of deep endometrial implants within the lymphovascular spaces and, from there, via the lymphatic drainage, to the regional lymph nodes [72]. There are no specific MRI features for endometriotic nodes [72].

Endometriosis associated with obstructive genital tract anomalies

Normally, menstrual blood flow exits the uterus via the cervical os; retrograde menstruation through the tubal ostia may occur in patients with severe outflow obstruction and may be associated with formation of hematosalpinges and implantation of endometriotic foci at the ovaries or deep in the pelvis [20,73]. Obstruction can occur at different levels of the genital tract, and may be congenital or acquired. Congenital obstructive reproductive tract disorders include the presence of a non-communicating uterine horn with functional endometrium (Fig. 19), cervical agenesis/dysgenesis, vaginal abnormalities (agenesis, transverse septum) or even an imperforate hymen. Although it is reported that the incidence of endometriosis is not higher in patients with Mullerian anomalies, endometriosis is strongly associated with obstructive malformations [74]. Therefore, endometriosis related to a reproductive tract anomaly, may be the cause of chronic pelvic pain in an adolescent patient [20]. Acquired cervical or isthmic stenosis as a postoperative complication (e.g. post-trachelectomy) may be yet another cause of severe outflow obstruction, potentially predisposing to secondary endometriosis [75]. MRI may readily demonstrate complications of genital tract outflow obstruction, such as hematosalpinx, hematomata, and/or hematosalpinx, as well as coexisting endometriosis (Figs. 20 and 21). In addition, MRI provides important information on the morphology of the female reproductive system and it exhibits high accuracy in localizing the site of obstruction along its course, potentially assisting surgical treatment [76].

Endometriosis in men

Endometriosis in a male is extremely rare. In most patients, it occurred in association with increased estrogen levels (prostate cancer under hormonal therapy, liver cirrhosis), presumably causing metaplasia of rests of Mullerian cells [77].

Endometriosis-related malignancy

Only a small percent of endometriotic lesions (<2.5%) undergo malignant transformation, most often those located at the ovaries (75%). Endometrioid or clear cell carcinomas are the most common subtypes arising in a preexisting endometriotic cyst; extra-adnexal endometriotic malignancy is of endometrioid sarcomatous histology. Women with endometriosis — related ovarian cancer are younger (at least 10–20 years) and have better prognosis than women who develop ovarian cancer without a history of endometriosis. Typical imaging features of malignant endometriomas, include the presence of a solid components within the endometriotic cyst (they usually appear as contrast-enhanced mural nodules), thick (>3 mm) internal septa, cyst enlargement on serial follow-up or loss of the T2 shading sign due to tumor secretions (Fig. 22); secondary features such as presence of ascites or peritoneal nodules often indicate malignancy. Tumor markers like CA-125 may be helpful for the discrimination between malignant and non-malignant endometriomas; although CA-125

Figure 19. 12-year-old adolescent presenting with catamenial pain. T2-weighted MR image in the axial plane demonstrates a typical banana-shaped unicorticate uterus (white arrow). A blood-filled non-communicating uterine horn is seen on the left (asterisk). Patients with obstructive genital tract malformations are at high risk for developing endometriosis.
Figure 20. 34-year-old woman presenting with prolonged and painful menstruation, two years after abdominal radical trachelectomy for cervical cancer. A. T2-weighted MR image in the sagittal plane clearly demonstrates the hemorrhagic fluid-fluid level within the distended endometrial cavity (small arrows) due to severe stenosis at the uterovaginal anastomosis (long arrow). B. T2-weighted MR image in the axial plane of the same patient shows concomitant right sided hematosalpinx (white arrow). The diagnosis of endometriosis was laparoscopically confirmed.

Figure 21. 24-year-old woman with vaginal agenesis but normal uterus and ovaries. A. T2-weighted MR image in the sagittal plane of the lower abdomen demonstrates a large cystic mass (black arrows) within the left rectus abdominis muscle. B. T1-weighted fat-suppressed MR image in the axial plane of the same patient shows high signal intensity of the mass consistent with subacute hemorrhagic content (white arrow). Pathological examination was diagnostic of endometrioma. Note the hemorrhagic fluid-fluid level within the distended non-communicating endometrial cavity (asterisk in A).

serum levels can also elevated in benign endometriosis, they are usually considerably higher in cases of malignancy [12,13,44].

Interestingly, recent studies report that patients with endometriosis seem to have an increased risk for developing type I (i.e. endometrioid) endometrial cancer. Additionally, there is some evidence that endometriosis may be related to breast cancer, particularly in patients with initial diagnosis of endometriosis at advanced age (≥ 50 years); however, data remain controversial and require further investigation [78].
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Figure 22. 39-year-old woman with no history of endometriosis, high Ca-125 and a right adnexal mass on routine ultrasound examination. T2-weighted MR image in the coronal plane shows a cystic and solid mass (black arrows) arising from the right ovary (white arrow). Histopathological examination of the surgical specimen revealed clear cell carcinoma with sarcomatous elements, arising from a preexisting ovarian endometrioma.

Conclusion

In endometriosis, the functional endometrium may be implanted in any tissue within or outside the pelvis and this results to a variety of clinical and imaging manifestations, which, in a considerable number of cases, may constitute a diagnostic challenge. Currently, MRI may be used as a problem-solving tool in cases of indeterminate adnexal findings on sonography, when deep infiltrating endometriosis is suspected, or for presurgical mapping. Knowledge of typical MR imaging features of endometriosis should help radiologists make the appropriate diagnosis. In cases with atypical locations, MRI findings combined with the history of catamenial symptoms may aid the diagnosis.

Disclosure of interest

The authors declare that they have no competing interest.

References


