Benign Uterine Lesions

5

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5.1 Uterine Leiomyomas: Background

5.1.1 Epidemiology

Leiomyomas, or fibroids, are the most common benign tumors of the uterus. The incidence of fibroids is difficult to estimate and frequencies reported in the literature range between 25% and 50%. In autopsy studies, leiomyomas of the uterus have been found in up to 77% of women [2, 21, 30]. Only about one third of affected women have fibroids that become clinically apparent before menopause. Fibroids may cause abnormal menstrual bleeding (menorrhagia with secondary anemia, dysmenorrhea) or pelvic pressure due to their mass effect (urinary frequency, constipation, pelvic pain, dyspareunia). Finally, leiomyomas of the uterus are also implicated in female infertility and are the most common indication for hysterectomy in western industrialized countries. In the USA 200,000 hysterectomies are performed for uterine fibroids each year [42, 47, 170].

Fibroids are smooth muscle tumors of the uterus that are influenced by steroid hormones and develop in women of reproductive age. They do not occur before puberty and fibroid-related symptoms become less severe or resolve altogether with the onset of menopause as a result of decreasing levels of steroid hormones (estrogen, progesterone) and cessation of the menstrual cycle. However, women on hormone replacement therapy may suffer from fibroid-related

complaints even after the sixth decade of life [153]. Hormonal stimulation during pregnancy can lead to considerable growth of fibroids and spontaneous infarction [29, 59]. Uterine fibroids are more common in black women compared with Caucasians or Asians. A black woman has a two to three times higher relative risk of developing fibroids than a white woman [114]. Reproductive factors also play a role. Fibroids are two times more common in nulliparous women as compared with women who have given birth and multiple pregnancies reduce the risk further [134, 162, 166]. Other factors associated with an increased risk (early menarche and late menopause, obesity, tamoxifen therapy) or reduced risk of leiomyoma development (smoking, low-meat diet) have been described [41, 47].

5.1.2 Pathogenesis

Our knowledge of the pathogenesis of uterine fibroids is still inadequate. Both genetic factors, steroid hormones and growth factors play a role in their development and growth. Two mechanisms involved in the development of fibroids can be distinguished: the initial neoplastic transformation of normal myocytes and the further increase in size under the influence of hormones and growth factors [47, 170]. While only little is known about the initial stimulus, it is undisputed that leiomyomas exhibit a variety of characteristic changes of the karyotype which give rise to a similar phenotype whose further growth occurs via clonal expansion [60, 198].

Estrogen and progesterone promote the development of leiomyomas whereas growth factors are assumed to act as mediators or effectors of these steroid hormones in leiomyomas [47, 48]. Estrogens are assigned a central role both in the development of leiomyomas and with regard to local effects resulting from a so-called leiomyoma-related hyperestrogenic environment. Compared to normal myometrium, fibroid tissue is more sensitive to estradiol, has more estrogen receptors, and an increased aromatase activity, which enhances the synthesis of estrogens within the fibroids [108, 164, 172, 192]. Finally, glandular hyperplasia of the endometrium has been demonstrated in the immediate vicinity of submucosal leiomyomas and is attributed to the effect of local hyperestrogenism [21]. Traditionally, estrogens were assumed to have the most important role in fibroid growth. Alternatively, it has been hypothesized that progesterones have a crucial role as it has been observed that the highest progesterone levels that occur during the secretory phase of the uterus coincide with the highest mitotic rate in leiomyomas [85, 154]. Many cytokines and growth factors stimulate fibroid growth [177]. These include transforming growth factor-ß (TGF-β), insulin-like growth factors 1 and 2 (IGF-1/2), basic fibroblast growth factor (bFGF), platelet-derived growth factor (PDGF), and epidermal growth factor (EGF) [176]. The expression of these factors is modulated by steroid hormones, suggesting that these factors are the ultimate effectors of the steroid hormones [207].

5.1.3 Histopathology

Leiomyomas are benign tumors arising from uterine smooth muscle cells. They typically develop in the uterine corpus or fundus but may also originate in the cervix (<8%) or rarely in the supporting structures of the uterus such as the broad ligament. So-called parasitic leiomyomas are no longer contiguous with the uterus and develop an atypical blood supply [88, 109, 217]. Two thirds of affected women have multiple fibroids. The majority of fibroids are seen as round lesions with a well-defined margin (Fig. 5.1). Growing fibroids displace the surrounding tissue, giving rise to a pseudocapsule of condensed myometrium, which allows surgical enucleation of the tumors. Macroscopically, the cut surface of leiomyomas has a whorl-like appearance. Histologically, leiomyomas are made up of intertwined smooth muscle cells arranged in fascicles forming whorl-like patterns (Fig. 5.2). These smooth muscle cells are embedded in a stroma of collagen fibers. Microscopically, the uniform cells have cigar-shaped nuclei and an eosinophilic fibrillary cytoplasm. The majority of fibroids show higher cell density than the surrounding myometrium. Mitosis and atypia are not found in fibroids. Histologically, different subtypes are distinguished, of which cellular and myxoid leiomyoma as well as lipoleiomyoma can also be differentiated by magnetic resonance imaging. Rare manifestations are diffuse leiomyomatosis of the uterus and forms that extend beyond the uterus. The latter comprise benign metastatic leiomyomatosis, peritoneal disseminated leiomyomatosis, and intravenous leiomyomatosis [62, 160, 189, 203]. Diffuse leiomyomatosis (Fig. 5.3) is characterized by the presence of many small ill-defined leiomyomas that may be confluent. The tumors are found

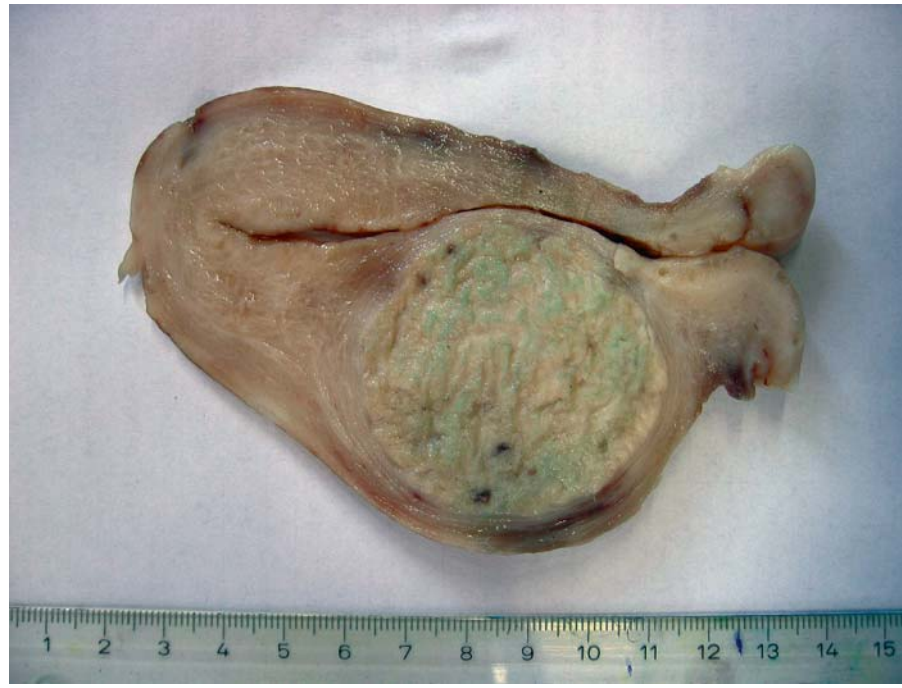


Fig. 5.1. Macroscopic pathology of leiomyoma. Macroscopic uterine specimen showing a single intramural leiomyoma in the wall of the uterine corpus abutting the endometrial cavity and deforming the outer contour of the uterus. A surrounding pseudocapsule of compressed myometrium can also be depicted

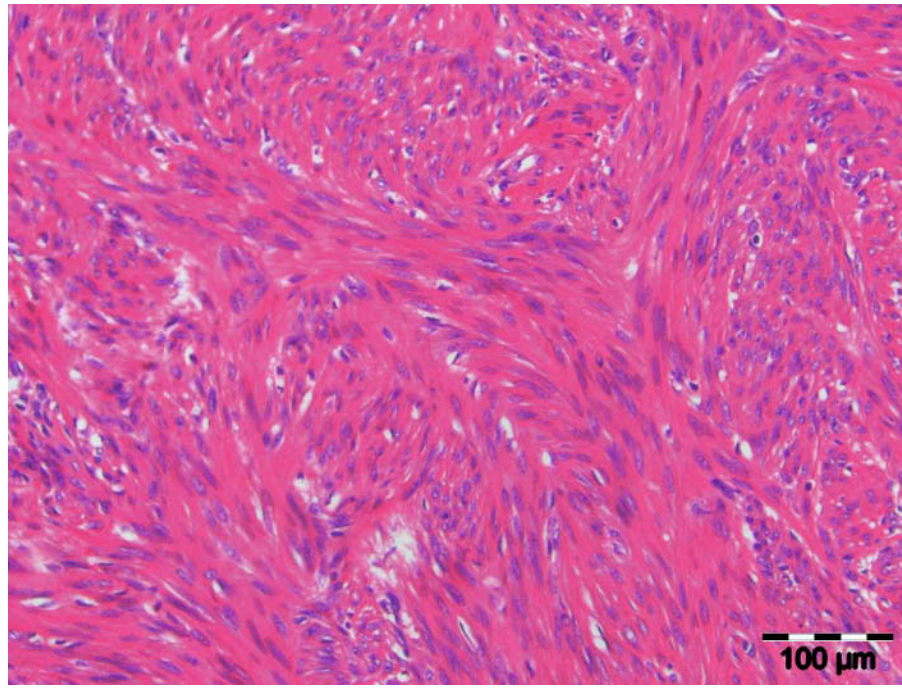


Fig. 5.2. Histopathology of uterine leiomyoma. H&E stained section of a leiomyoma specimen showing monomorphic smooth muscle cells arranged in fascicles forming whorl-like patterns

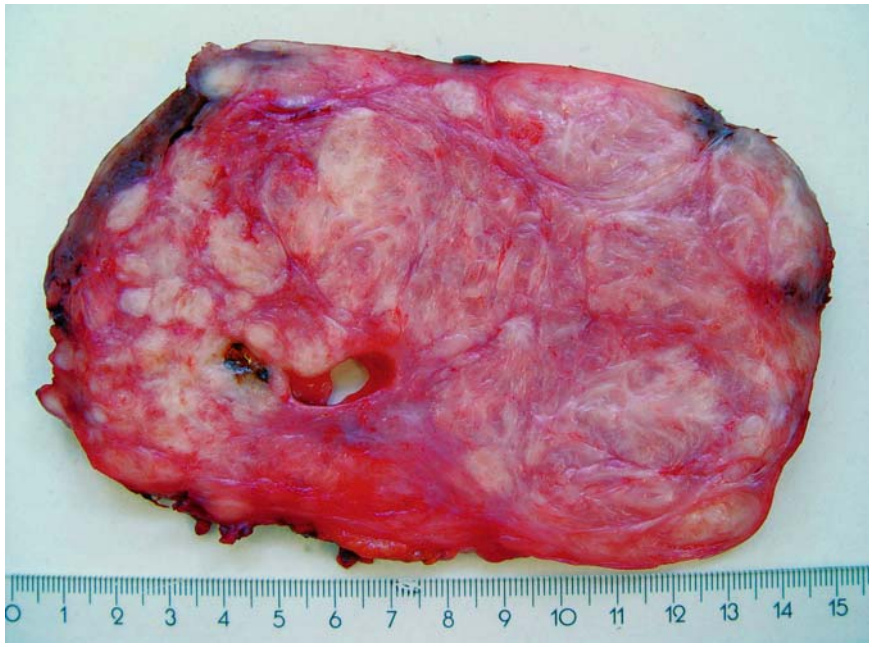


Fig. 5.3. Macroscopic pathology of diffuse leiomyomatosis of the uterus. Macroscopic uterine specimen showing multiple ill-defined leiomyomas throughout all uterine layers ranging from millimeters to several centimeters in size. The leiomyomas are partially confluent and have replaced almost the entire normal myometrium, a condition also known under the term of (diffuse) leiomyomatosis

throughout the myometrium and cause symmetrical enlargement of the uterus [125, 161].

Another factor contributing to the very heterogeneous imaging appearance of uterine fibroids is the presence of degenerative changes. Fibroids undergo degeneration when the tumors outgrow their blood supply. Typical degenerative changes such as hyaline degeneration, which is present in over 60% of leiomyomas, as well as hemorrhagic (red), myxoid, and (rare) cystic degeneration (4%) can be differentiated by MRI [220]. Other typical changes are amorphous or plaque-like calcifications, which are present in 3%–8% of leiomyomas [24]. Most of the fibroid subtypes that can be distinguished histologically or by imaging as well as the degenerative changes outlined above have no clinical relevance for therapeutic decision-making. An exception is hemorrhagic infarction of a fibroid during pregnancy, which is identified by MRI in a straightforward manner [59]. Criteria that are used for the differentiation of a leiomyosarcoma from fibroids include an increased mitosis rate, the presence of cytologic atypia as well as the presence of coagulation necrosis with or without intralesional hemorrhage [11, 54, 77, 87]. Hemorrhage and necrosis within leiomyomas only occur in the rare cases of spontaneous or pregnancy-related hemorrhagic infarction but are common early after interventional therapy by means of uterine artery embolization (UAE). Postinterventional hemorrhage and necrosis may in this setting affect large portions or the whole leiomyoma [211].

5.1.4 Clinical Presentation

Leiomyomas of the uterus are rare under the age of 30; they typically become manifest during the fourth to sixth decades of life. Typical symptoms are excessive and/or prolonged menstrual bleeding (hypermenorrhea and menorrhagia). Bleeding between periods or irregular bleeding may be observed in patients with pedunculated submucosal fibroids but is not characteristic and therefore requires diagnostic evaluation of the endometrium (endometrial biopsy, dilatation and curettage). Women with heavy periods frequently develop iron deficiency anemia. Other frequently reported complaints are bulk symptoms manifesting as a premenstrual sensation of fullness (increased abdominal/pelvic girth), urinary urgency, and indigestion. Affected women usually complain of painful periods (dysmenorrhea), less common is unspecific pain radiating into the flank or the back, or pain during intercourse (dyspareunia). These symptoms alone are not characteristic of uterine fibroids and must be interpreted in conjunction with a patient's history and imaging findings.

A patient's symptoms vary with the location and size of the fibroids. For example, submucosal fibroids can cause severe menstrual bleeding even when they are very small. In women with this type of fibroid, abnormal menstrual bleeding is attributed to ulceration and rarefaction of the endometrium over the fibroid due to compression, reduced uterine contractility, and

congestion of endometrial veins. Intramural fibroids are associated with an especially high incidence of abnormal and painful menstrual bleeding.

In patients presenting with dysmenorrhea as the leading clinical symptoms, the examiner should always consider uterine adenomyosis and endometriosis in the differential diagnosis [219]. Subserosal fibroids can become very large without causing any symptoms. Compression of the intestine and urinary bladder with urinary frequency or urgency, and abdominal bloating around periods are more commonly associated with subserosal fibroids. Moreover, there is increasing evidence suggesting that symptoms are not only due to merely mechanical local effects, but that additional factors associated with specific biological activities of the fibroids also play a considerable role. Such functional factors influence the subendometrial vascular bed through dysregulation of growth and angiogenic factors and are primarily implicated to cause fibroid-related abnormal menstrual bleeding [32, 187].

The impairment of quality of life caused by fibroid-related problems and the measurable loss of economic productivity due to absence from work are considerable. For the US it has been estimated that at least 5 million workdays are lost per year due to fibroids and that the annual treatment cost amounts to US$ 3 billion [56]. The high incidence of fibroids and its socioeconomic implications as well as individual loss of quality of life are in sharp contrast to our still limited understanding of the pathogenesis of uterine fibroids and inadequate therapeutic options. A lack of research into the epidemiology, pathogenesis, and pathophysiology of leiomyomas of the uterus as well as their "benign nature" are the most important factors that have so far inhibited the search for alternative therapeutic options to replace the radical surgical approach of hysterectomy [126]. Surgical removal of the uterus continues to be the most widely used therapeutic approach in patients with symptomatic fibroids. In Western industrialized countries, uterine fibroids are the most frequent indication for removal of the uterus, accounting for 200,000 hysterectomies per year in the US alone [42, 47, 170]. One in five women in Great Britain will undergo hysterectomy before the age of 55 with 90% of all hysterectomies being performed for uterine leiomyomas [40, 206]. Only recently – and not least of all because more and more affected patients are asking for alternative nonsurgical, uterus-sparing therapies – has research interest in this area focused on the stratification of therapy and the scientific evaluation of alternative therapeutic options such uterine artery embolization [3].

5.1.5 Therapy

5.1.5.1 Indications

Treatment of uterine fibroids is indicated when they cause symptoms [3] while a wait-and-see approach is in order in women without symptoms. Whether treatment is indicated or not does not depend on the size of the uterus or that of individual fibroid tumors since there is no evidence that marked enlargement of the uterus is associated with an increased surgical morbidity. Traditionally, rapid growth of a fibroid has been interpreted as a sign of malignancy (leiomyosarcoma), while the results of larger studies do not confirm this assumption [106, 137]. When deciding about hysterectomy for exclusion of potential leimyosarcoma (prevalence: 1:2000), one has to critically weigh the benefit against the surgical mortality rate (1.0–1.6:1000) [3]. More recent studies suggest that transcervical needle biopsy in combination with enzyme marker determination (LDH) and MRI can contribute to therapeutic decision-making [87]. A relative indication for treating asymptomatic leiomyomas exists in women who want to conceive and have a history of miscarriage and proven fibroid-related deformity of the uterine cavity. In these cases treatment is indicated because the fibroids can interfere with placentation and pregnancy is associated with additional risks [59, 143, 146, 159].

5.1.5.2 Medical Therapy and Ablation

Medical therapy is usually symptomatic and aims to relieve fibroid-related abnormal menstrual bleeding (hypermenorrhea, menorrhagia), dysmenorrhea, and bulk symptoms. Oral contraceptives of different hormonal composition and nonsteroidal anti-inflammatory drugs with analgesic and antifibrinolytic effects are used, although evidence for their long-term effectiveness in treating uterine fibroids is not available [126, 186]. Moreover, there is no data demonstrating a growth-reducing effect of oral contraceptives. These therapeutic options are used in the routine clinical setting to bridge the time until definitive therapy is performed. Treatment with GnRH analogues improves fibroid-related symptoms and leads to a transient reduction of fibroid size. Maximum size reduction is seen after about 3 months of treatment. Once GnRH analogues are discontinued, however, leiomyomas will again increase in size. This is why

GnRH analogues are given only to reduce leiomyoma size prior to surgery [218]. GnRH administration is also beneficial to minimize blood loss in case of larger fibroids or for the transient treatment of anemia resulting from heavy menstrual bleeding. However, GnRH treatment causes softening of fibroids, which is a disadvantage for surgical enucleation.

The severity of menstrual bleeding can be reduced by insertion of a *levonorgestrel-releasing intrauterine device* (IUD) [123, 213]. The effect of such IUDs is based on the local activity of continuously released progesterone, which effectively suppresses the endometrium. While data from larger studies regarding risks, adverse events and the long-term effectiveness in patients with multiple leiomyomas of the uterus is lacking, it is known that an IUD for the treatment of hypermenorrhea has a higher failure rate in the presence of submucosal fibroids [213].

Endometrial ablation is a permanent and invasive therapeutic option which relieves excessive menstrual bleeding in 62%–79% of cases [175]. Thermoablation of the endometrium is performed using a balloon or roller ball technique and a hysteroscopic access. The success of endometrial ablation in the presence of fibroids is small since not the entire endometrium is accessible in women with multiple leiomyomas because of enlargement and deformity of the uterine cavity.

5.1.5.3 Surgical Therapy

Hysterectomy is a definitive cure in patients with a symptomatic multifibroid uterus. Both abdominal and vaginal hysterectomy is associated with a low mortality and morbidity. However, given that uterine leiomyomas are benign lesions, the large number of hysterectomies performed worldwide to treat this condition appears to be disproportionate [16]. As an alternative to hysterectomy, uterus-sparing operative, ablative, and interventional radiological procedures are available, depending on location and size of fibroids present, the patient's age, desire to have children, and personal preferences.

Depending on their location, leiomyomas can be resected or enucleated using a hysteroscopic or laparoscopic access or open laparotomy. Hysteroscopic resection is suitable to remove submucosal leiomyomas. Hysteroscopic resection is generally considered unsuitable for submucosal leiomyomas larger than 5 cm in size, if more than three fibroids are present, or if the uterine cavity is very large (length of uterine probe > 12 cm). Moreover, the size of the intramural component is a risk factor of the hysteroscopic resection because the risk of perforation increases when the residual myometrium is thin [210]. The rate of repeat interventions necessary after hysteroscopic fibroid resection is reported to range from 16%–21% for a follow-up period of 4–9 years [31, 58]. Fewer repeat interventions are required (8%) when hysteroscopic fibroid resection is combined with ablation of the endometrium [205].

A laparoscopic access is used to remove visible subserosal and intramural leiomyomas in combination with reconstruction of the uterus. This approach is unsuitable in the presence of very large fibroids or a markedly enlarged uterus because these factors limit the use of the laparoscope and visibility. Using the laparoscopic approach, multiple fibroids can be enucleated in one session. Visible fibroids can be removed while intramural tumors are not easily accessible to laparoscopic removal. Incision of the uterine cavity necessary for the removal of transmural fibroids is considered a disadvantage because it is associated with the risk of synechia. Adhesions are observed in 33%–54% of patients following laparoscopic interventions [35, 61, 110]. The risk of recurrence after laparoscopic fibroid removal is up to 50% in women followed up for up to 5 years [34, 127]. Laparotomy is primarily used in patients with one or more large fibroids, which are removed using an adjusted abdominal incision. The perioperative risks of laparotomy are comparable to those of hysterectomy while the rate of adhesions may be as high as 90% [167, 202]. The recurrence rate after abdominal myomectomy is 10% within 5 years and up to 27% after 10 years. One third of the patients with recurrent leiomyomas will ultimately undergo hysterectomy [23, 43].

5.1.5.4 Uterine Artery Embolization (UAE)

Uterine artery embolization (UAE) is an established technique that has been used to stop life-threatening vaginal hemorrhage in women with malignancy, postpartum uterine atony, or traumatic injury since the mid-1970s [8, 18, 52, 64, 112]. The first successful treatment of symptomatic fibroids of the uterus by UAE was reported by Ravina et al. in 1994 [150].

Embolization of the uterine artery induces infarction of fibroids while uterine perfusion is maintained [84, 119]. Infarction leads to coagulation necrosis and subsequent complete hyalinization of the fibroids [27, 119, 211]. Further transformations cause softening and shrinkage of the tumors. Follow-up for 3–24 months has shown that there is an average size reduction of the uter-

us of 23%–60%, while the dominant fibroid decreases by 42%–78% on average. Progressive shrinkage of the fibroids has been documented for a period of 12 months [19, 70, 101, 120, 147, 148, 179, 209]. Several studies provide evidence for a relief of bleeding-related symptoms in 80%–100% of patients and a regression of bulk symptoms in 60%–100% of patients followed up for 3–60 months [4, 19, 70, 83, 101, 120, 147, 148, 179, 209]. Studies comparing UAE with hysterectomy and myomectomy in the treatment of symptomatic uterine leiomyomas suggest that UAE has a similar success rate in terms of symptom relief and patient satisfaction, while it has a lower complication rate and shorter recovery period as compared with the surgical procedures [15, 111, 152, 182]. These results are confirmed by two randomized studies [63, 144]. Only few investigators report long-term results after UAE but the available data suggests that permanent improvement of symptoms can be expected in two thirds of women [15, 181]. Complications during the intervention are extremely rare [100, 185]. Following UAE, 5%–10% of the patients report vaginal discharge with or without tissue passage and expulsion of infarcted fibroids may occur [1, 13, 98, 136]. Fibroid expulsion occurs weeks to months after the intervention and may necessitate administration of antibiotics and pain medication if complicated by superinfection and, in rare cases, surgically assisted removal or hysteroscopic resection [70, 120, 179]. Transient amenorrhea persisting for up to three cycles is not unusual while permanent amenorrhea is rare and occurs more commonly in patients over 45 years than in younger ones [26, 200, 209]. UAE can be performed in patients with single or multiple fibroids but, based on current knowledge, patients who wish to preserve their fertility should be treated by UAE only if alternative, uterus-sparing therapeutic approaches have been attempted or are not an option. All uterus-sparing therapeutic approaches share the risk of newly occurring fibroids and may require repeat interventions or hysterectomy due to complications of surgical or interventional treatment.

5.2 Adenomyosis of the Uterus

5.2.1 Epidemiology

Adenomyosis (endometriosis genitalis interna) of the uterus affects premenopausal women and is predominantly seen in multiparous women and women over 30 years of age [9, 135]. Because its symptoms are unspecific, adenomyosis rarely comes to clinical attention, which is why the incidence of this uterine condition is underestimated [9]. Until recently, the diagnosis was established almost exclusively after hysterectomy. Histologic examination of hysterectomy specimens demonstrates adenomyosis in 19%–63% of cases [9]. Adenomyosis often occurs in conjunction with fibroids and endometriosis (endometriosis genitalis externa et extragenitalis) [103, 219].

5.2.2 Pathogenesis

Adenomyosis is a nonneoplastic condition which results from the dislocation of basal endometrial glands and stroma into the underlying myometrium [46]. It has been shown that adenomyosis progresses with age, suggesting that there is continuous progression from superficial to deep myometrial involvement [102]. The dislocated endometrial glands in adenomyosis do not undergo cyclic changes, which has been attributed to the predominance of the zona basalis in these glands [9]. The mechanism underlying the dislocation of basal endometrium is largely unknown. Estrogen-mediated and mechanical effects seem to play a role. Since adenomyosis is seen predominantly in parous women, a breakdown of the basal layer of the endometrium and myometrium due to postpartum endometritis has also been proposed as a possible cause [173].

5.2.3 Histopathology

Adenomyosis presents morphologically as focal areas or diffuse involvement of the uterus. Grossly, the cut surface is characterized by a whorled texture which results from the irregular trabeculations of the thickened myometrium (Fig. 5.4). Another common feature are cyst-like lesions. Hemorrhagic foci within the myometrium may also be seen on gross inspection. The diagnosis is based on the histologic demonstration of dispersed endometrial glandular tissue in the myometrium and requires the presence of at least one glandular nest at a depth of more than 2.5 mm or one-half of a low-power field (×100) within the myometrium measured from the endomyometrial junction [220]. The islets of glandular tis-

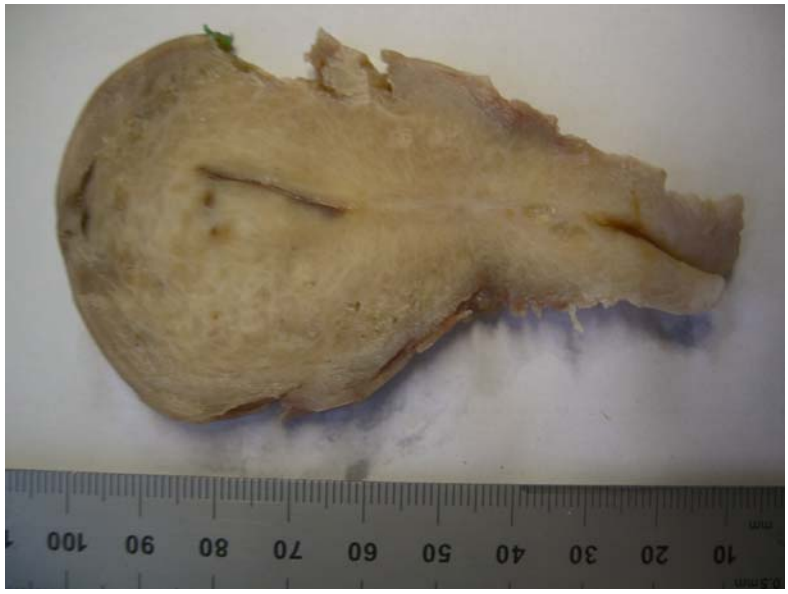


Fig. 5.4a,b. Macroscopic pathology of adenomyosis of the uterus. **a** Macroscopic uterine specimen showing focal adenomyosis. A thickened anterior uterine wall with broadening of the myometrium as well as irregular myometrial trabeculations and multiple micro-cysts are visible. **b** Magnified area of the anterior uterine wall showing coarse trabeculation of the myometrium without a mass lesion and small brownish cysts corresponding to hemorrhagic foci of dislocated endometrial glands

sue are surrounded by hypertrophied myometrium (Fig. 5.5). Pathologically a superficial form of adenomyosis which only involves the inner myometrium can be differentiated from deep-infiltrating adenomyosis which considerably enlarges the uterine wall due to smooth muscle hyperplasia adjacent to deep-infiltrating endometrial glands [46].

5.2.4 Clinical Presentation

The clinical presentation of adenomyosis is unspecific and includes symptoms such as dysmenorrhea, menorrhagia, and pelvic pain, which are also common in disorders like dysfunctional bleeding, leiomyoma, and endometriosis. The uterus is frequently enlarged in women with adenomyosis but not distorted in its shape like with uterine leiomyoma. Women with superficial or focal adenomyosis may be asymptomatic in contrast to women with extensive disease in whom the uterus usually is also markedly enlarged. The depth of involvement of the uterine wall correlates to some degree with clinical symptoms [12, 14, 117]. Dysmenorrhea has been reported to be more frequent when involvement of the myometrium by adenomyosis exceeds 80% of the diameter of the uterine wall [128].

5.2.5 Therapy

Hysterectomy is still considered the definitive treatment in patients with symptomatic adenomyosis. However, initially less invasive therapeutic options

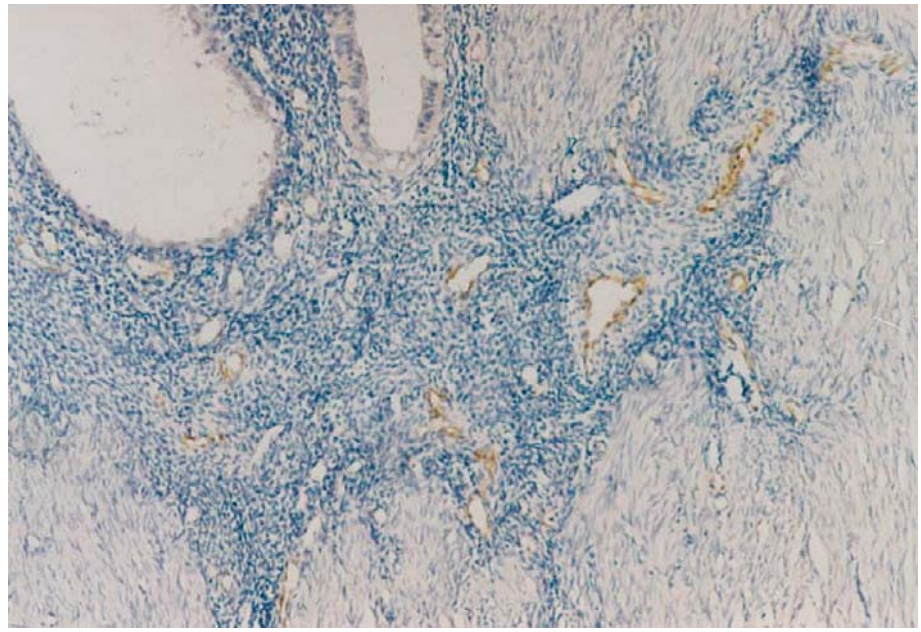


Fig. 5.5. Histopathology of adenomyosis of the uterus. Dislocated endometrial glands are surrounded by hypertrophied myometrium. (Reproduced with permission from [222])

should be considered taking into account the patient's age, symptom severity, and desire of future fertility, as well as the presence of associated disorders such as leiomyomas and endometriosis. Symptom relief can be achieved with nonsteroidal anti-inflammatory drugs, but suppression of the endometrium by hormonal treatment with danazol or gonadotropin-releasing hormones (GnRH) may be needed. Intrauterine devices (IUD) which release levonorgestrel have been shown to be effective in controlling menorrhagia caused by adenomyosis although symptoms return once the IUD is removed [45]. Endometrial ablation or resection denudes the endometrial layer of the uterus and is an option for women with predominantly abnormal uterine bleeding. Adenomyosis of the superficial type with less than 2 mm penetration responds better than deep-infiltrating adenomyosis to endometrial ablation [118].

Uterus-conserving surgery is hampered by the lack of a clearly defined dissection plane but may be of value in the infertile patient [133]. Laparoscopic resection of adenomyosis has been shown to reduce pain, menorrhagia, and dysmenorrhea in small case series with limited follow-up [124, 214]. Recently, uterine artery embolization (UAE) has been reported to be successful in relieving menorrhagia and dysmenorrhea at short-term. The long-term benefit of UAE in patients with adenomyosis is still under investigation [93, 94, 141, 174].

5.3 Imaging

5.3.1 Diagnostic Imaging for Uterine Leiomyomas and Adenomyosis – An Overview

Uterine leiomyomas and adenomyosis cannot be reliably differentiated on clinical grounds because both conditions cause similar symptoms.

Leiomyomas of the uterus, once they have reached a certain size, can be palpated and differentiated from the uterine wall as solid tumors that tend to be mobile. Bimanual palpation is typically supplemented by transvaginal ultrasound (TVUS) or, in patients with a markedly enlarged uterus, transabdominal ultrasound. The ultrasound examination allows assessment of the uterus and especially TVUS provides additional information on the endometrium and ovaries. TVUS is the primary imaging modality in the diagnostic work-up of women with uterine leiomyomas. Ultrasound depicts fibroids as hypoechoic round lesions which are sharply demarcated from the remainder of the uterus (Fig. 5.6). Anechoic cystic portions and degenerative changes with a heterogeneous echo pattern within the lesions are quite common. US enables reliable assessment of the location of fibroids and their topographic

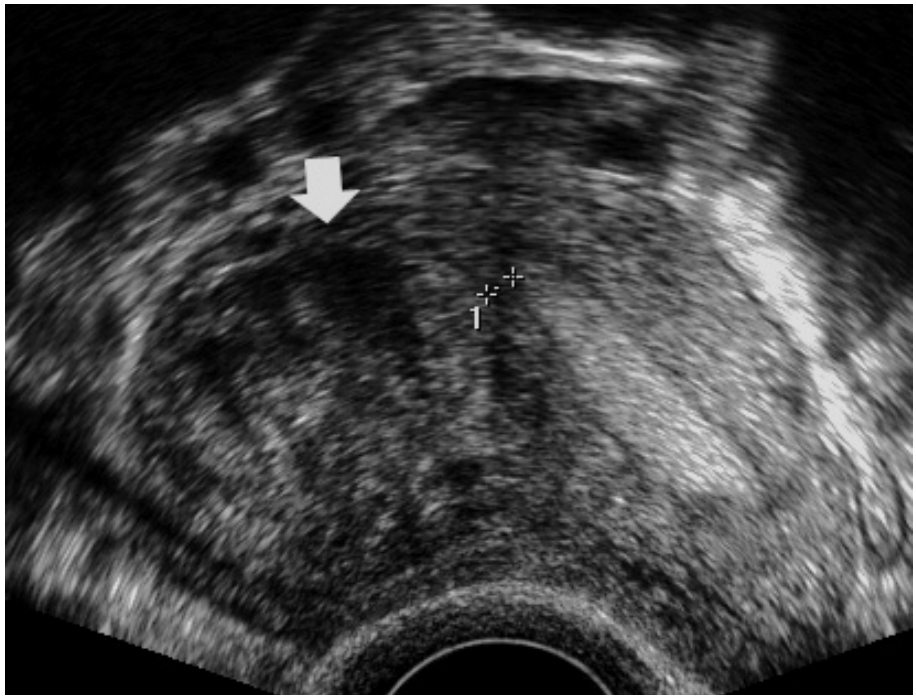


Fig. 5.6. Transvaginal ultrasound (TVUS) of uterine leiomyoma. TVUS demonstrates a well defined subserosal leiomyoma (*arrow*) distorting the outer contour of the uterine wall. The leiomyoma shows a heterogenous echotexture and is hypoechoic compared to the adjacent myometrium and endometrium. The endometrium is seen as a hyperechoic stripe

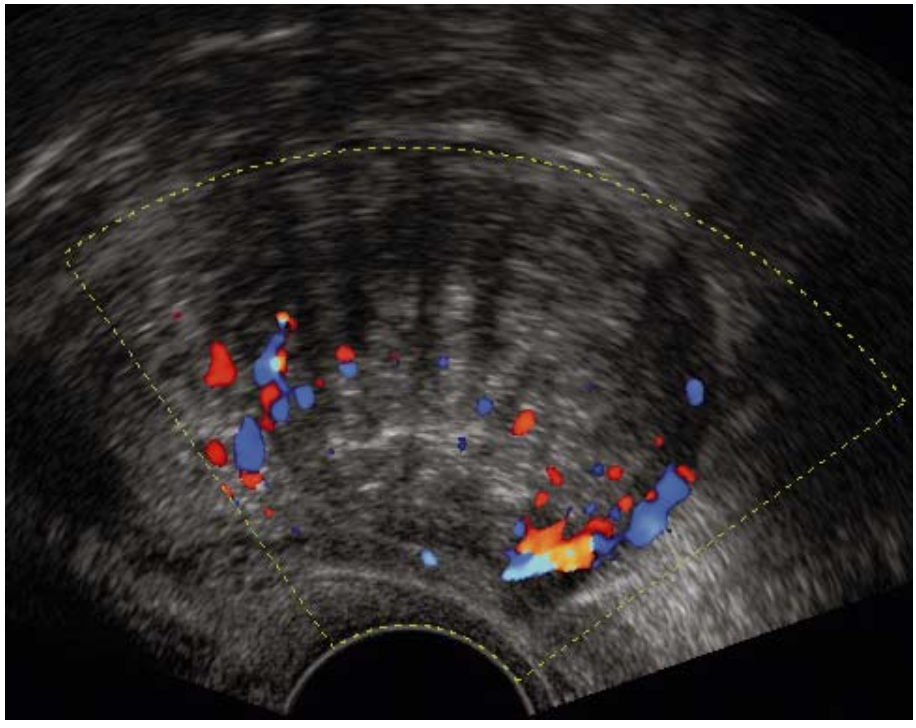


Fig. 5.7. Transvaginal ultrasound of leiomyoma. Transvaginal color-coded duplex ultrasound demonstrates the perifibroid plexus vessels surrounding the leiomyoma

relationship to surrounding structures, and in particular the uterine cavity, in most cases. Additional color-coded duplex ultrasound will depict tumor vascularity and demonstrate typical features such as a central vessel or a marginal vascular network (Fig. 5.7). Hysterosonography with the instillation of fluid into the uterine cavity improves the diagnostic accuracy of TVUS in detecting submucosal fibroids, differentiation from endometrial polyps, and determining depth of myometrial (uterine wall) involvement [38].

Endoscopic procedures such as laparoscopy or hysteroscopy have a role in patients with suspected fibroids and inconclusive US findings. Moreover, hysteroscopy is performed in conjunction with endometrial sampling in women with abnormal menstrual bleeding and for specific diagnostic purposes such as evaluation of the uterine cavity and tubes in infertile women with fibroids. In patients with known uterine leiomyomas, laparoscopy and hysteroscopy have their main role as therapeutic procedures for the uterus-sparing resection of known uterine fibroids.

Magnetic resonance imaging (MRI) is the most accurate diagnostic modality for assessing uterine leiomyomas [37]. MRI enables assessment of the uterus in multiplanar orientation and without interference from superimposed structures. MRI provides not only accurate information on the number and size of fibroids but also on their location within the uterus (cervix, corpus, fundus) and within the wall (submucosal, intramural, subserosal), as well as their relationship to neighboring structures such as the tubes and ovaries (Figs. 5.8 and 5.9). The unique soft tissue contrast afforded by MRI enables good delineation of the fibroid tumors from adjacent myometrium, the junctional zone, which is important for the differential diagnosis, and the endometrium and also enables evaluation of the internal make-up of fibroids including secondary degenerative changes. These features thus make MRI superior to all other imaging modalities in characterizing uterine fibroids. MRI is of use in patients with inconclusive US findings with regard to the differential diagnosis of a pelvic lesion or the origin of a lesion from the uterus or the ovary [171, 212]. MRI is increasingly being used to evaluate the feasibility of uterus-sparing surgical therapy or a radiologic intervention [36]. To establish the indication for hysteroscopic or laparoscopic resection, it is necessary to know the number and size of fibroids as well as their precise position, in particular their relationship to the uterine cavity and their depth within the wall [39, 68]. In evaluating potential candidates for UAE, MRI provides information on the size of the individual fibroids, the presence of pedunculated or parasitic leiomyomas, the nature of degenerative changes, the degree of fibroid vascularization and the vascular supply of the uterus.

Computed tomography (CT) with its poor soft tissue contrast is of limited value in diagnosing benign changes of the uterus. CT does not allow adequate differen-

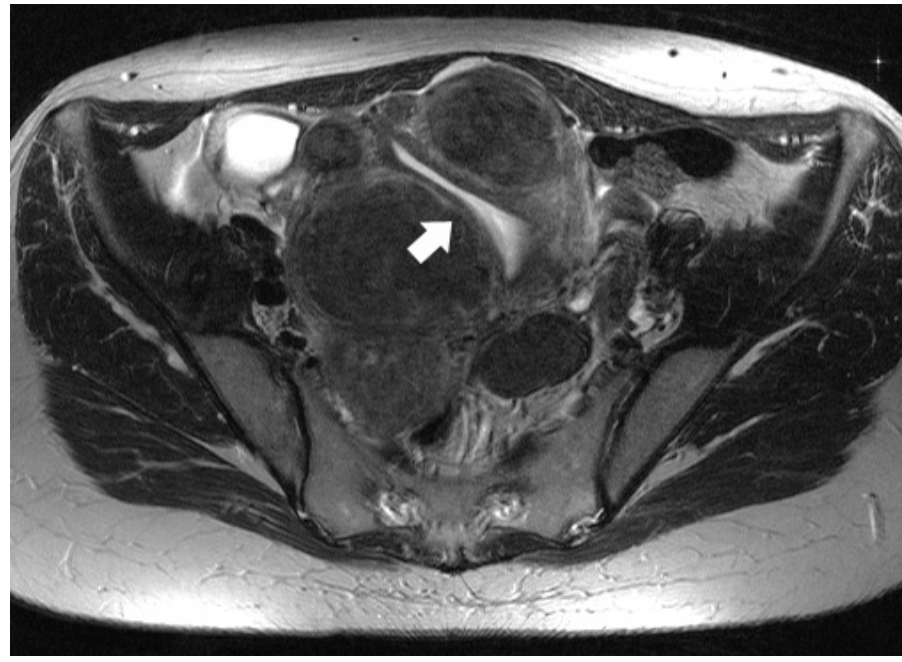


Fig. 5.8. MRI of leiomyoma – locations. Transaxial T2-weighted image depicts multiple, mainly subserosal uterine leiomyoma. There is mild distortion of the uterine cavity by a transmural (full thickness) leiomyoma (*arrow*)

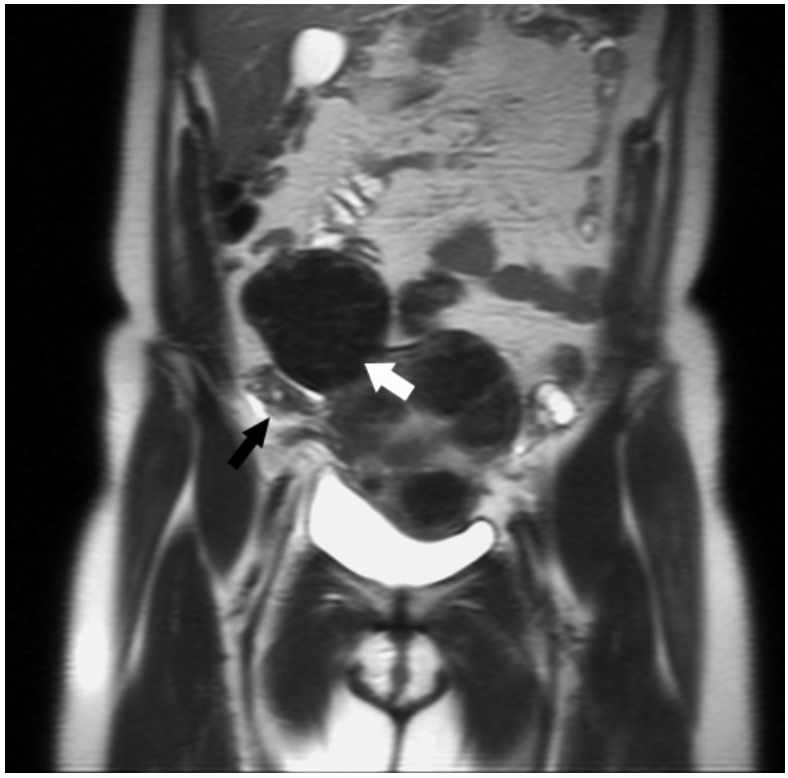


Fig. 5.9. MRI of leiomyoma – locations. T2-weighted coronal image of a polyfibroid uterus. A subserosal pedunculated uterine fibroid (*white arrow*) is easily identified by its low signal intensity and continuity with the right lateral aspect of the uterine fundus while sonographically the lesion could not be separated from the right ovary (*black arrow*). (Reproduced with permission from [223])

tiation of the different uterine layers and hence fails to reliably assign uterine lesions to a specific layer. Intravenous contrast medium administration improves the differentiation of adjacent structures but does not improve the differential diagnosis (Fig. 5.10). On CT scans, uterine fibroids are isodense with muscle and can occasionally be identified by the presence of typical calcifications on unenhanced images. There are no specific CT criteria for the presence of adenomyosis.

Adenomyosis – when severe – causes enlargement of the uterus but differs from fibroid-related enlargement in that the uterus is soft on palpation. TVUS will depict areas of reduced echogenicity or a heterogeneous appearance in about 75% of patients with adenomyosis [17, 44, 155]. Apart from asymmetric thickening of the myometrium in the presence of focal adenomyosis, other morphologic features that are indicative of adenomyosis are a poor definition of the endomyometrial junction, the presence of myometrial cysts (< 5 mm) in up to 50% of affected patients, as well as echogenic lines or spots within the myometrium [44, 72]. Circumscribed lesions are absent in the majority of cases. Good diagnostic performance can be expected if diagnostic criteria as described above are combined and real-time examination is used. An increased vascularization demonstrated by color duplex US is indicative of adenomyosis [25, 65]. Transvaginal ultrasound has a reported sensitivity of 53%–89% and a specificity ranging from 50%–99% [6, 17, 44, 155]. The wide variation is primarily attributable to the examiner dependence of US. The diagnostic accuracy is limited in the presence of fibroids [10]. Many of the features of adenomyosis seen on US are depicted more clearly on T2-weighted MR images, which clearly show changes in zonal anatomy based on the excellent soft tissue contrast of this imaging modality (Fig. 5.11). Despite its sensitivity of 86%–100% and specificity of 85%–90.5% for the diagnosis of adenomyosis and its high diagnostic accuracy in establishing the differential diagnosis, MRI is rarely used in the routine clinical setting, for two reasons: adenomyosis is rarely suspected as the cause of hypermenorrhea or dysmenorrhea before surgery and reliable pretherapeutic demonstration of adenomyosis as the underlying cause in symptomatic women in the fourth or fifth decades of life was considered irrelevant for therapeutic decision-making (hysterectomy) [6, 113, 156, 195]. MRI is thus not indicated and cost-effective in the initial evaluation of patients with unspecific complaints suggestive of adenomyosis. However, MRI has its place as an ad-

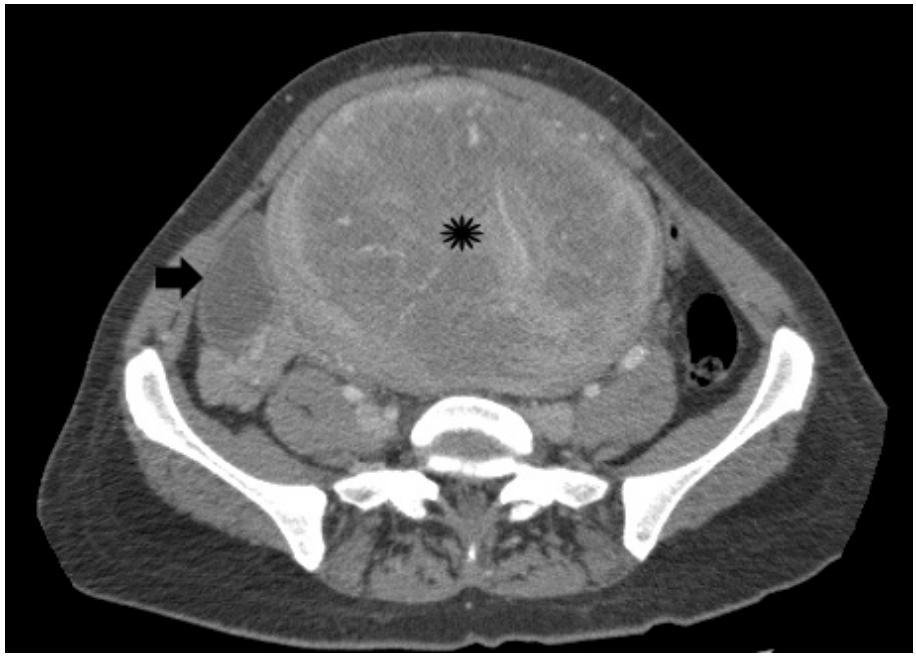


Fig. 5.10. CT of uterine leiomyoma. Contrast-enhanced CT of the pelvis in a 39-year-old women with a known uterine leiomyoma shows a large oval mass within the uterus with heterogenous enhancement (*asterisk*) which displays the hypodense right ovary (*arrow*) and distends the abdomen

junctive tool in patients with diffusely enlarged uteri of unknown cause, in the work-up of infertile women, and for follow-up of patients receiving GnRH therapy for adenomyosis or prior to uterus-conserving surgical therapy and UAE [71, 90, 93, 133].

5.3.2 Magnetic Resonance Imaging

5.3.2.1 Magnetic Resonance Imaging – Technique

A short clinical history including menstrual status, previous pelvic surgery, clinical symptoms, time point within the menstrual cycle, and current hormonal therapy should be taken prior to an MR examination of the female pelvis. Due to the cyclic changes of the uterus, imaging is best performed in the second half of the menstrual cycle to take advantage of maximum signal differences between the uterine layers. The pelvis should be imaged on a high-field (1.5-T) scanner using a pelvic or torso phased-array coil. Motion artifacts caused by bowel peristalsis can degrade image quality significantly and should be eliminated. Measures to reduce such artifacts include asking the patient to fast for 4–6 h prior to the examination and intramuscular injection of butylscopolamine in patients who have no contraindications. Patients should also be instructed to void prior to the examination. The standard protocol for pelvic MR imaging should include both T1- and T2-weighted sequences. Breath-hold T2-weighted sequences acquired in the true axial, sagittal, and coronal planes (T2-HASTE, SSFSE) are sufficient to diagnose uterine leiomyomas and adenomyosis in the majority of cases [7, 115]. However, the relationship of a uterine lesion to the uterine cavity may be difficult to recognize on breath-hold images alone. Additional high-resolution (512-matrix) T2-weighted TSE sequences acquired in the axial and sagittal planes in conjunction with presaturation of the anterior abdominal wall are recommended in cases of inconclusive breath-hold images or a severely distorted uterine cavity [215]. T1-weighted pulse sequences with and without fat saturation acquired in the axial plane provide information on fatty components and blood products within a lesion and accentuate areas of calcification otherwise not seen on T2-weighted imaging. Gadolinium-enhanced T1-weighted images can provide additional information on the vascularity of uterine leiomyomas, improve the visualization of the surrounding pseudocapsule, and may help to delineate the uterine origin of a subserosal leiomyoma, but are not necessary to diagnose uterine leiomyomas and adenomyosis [67]. However, additional MRA gradient-echo sequences are recommended in patients with leiomyomas and adenomyosis in whom uterine artery embolization is planned [99].

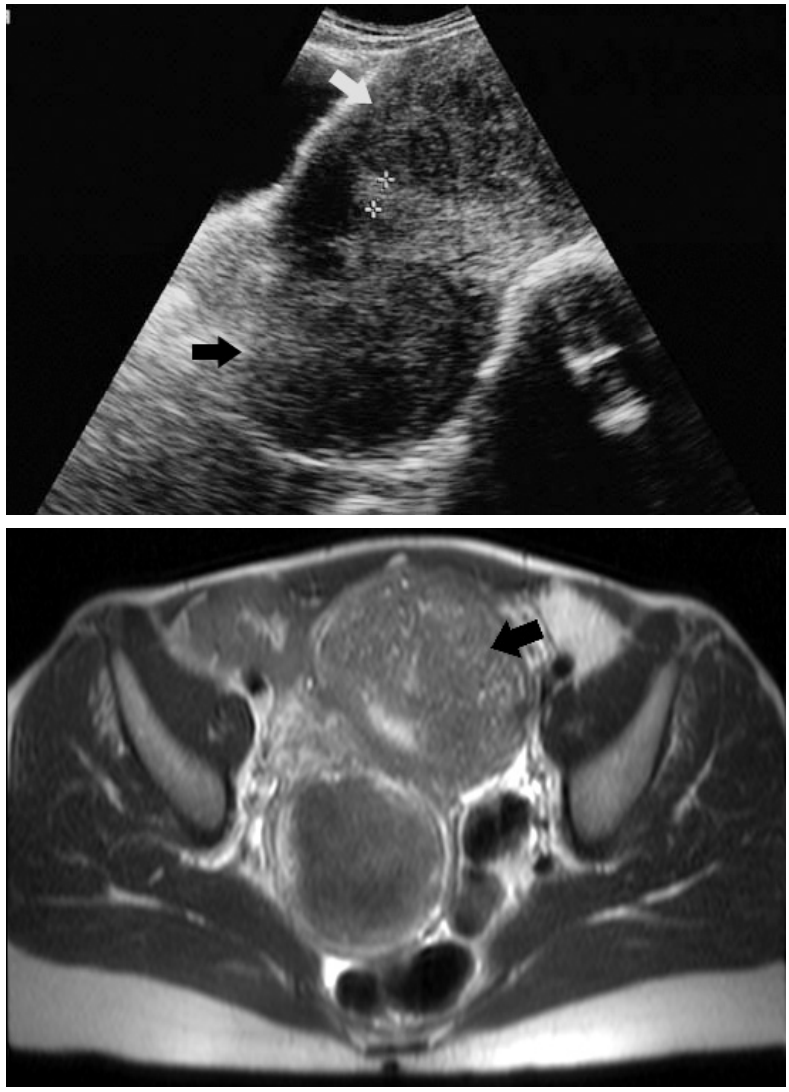


Fig. 5.11a,b. Correlation of transvaginal ultrasound (TVUS) and magnetic resonance imaging (MRI) in a patient with leiomyoma and adenomyosis of the uterus. **a** TVUS of a 48-year-old women with menorrhagia and dysmenorrhea. Two leiomyoma were reported to be present, one in a subserosal location (*black arrow*) of the posterior wall and a second intramurally in the anterior uterine wall (*white arrow*). However, a poor definition of the endomyometrial junction and asymmetric myometrial thickening of the anterior uterine wall rather than a clear mass lesion is seen. Calipers indicate measurement of endometrial thickness. **b** Corresponding T2-weighted transaxial image shows a subserosal leiomyoma of the posterior uterine wall and focal adenomyosis of the anterior uterine wall (*black arrow*) characterized by a broadening of the junctional zone and cyst-like inclusions in the myometrium corresponding to endometrial glands

5.3.2.2 MR Appearance of Uterine Leiomyomas

Leiomyomas of the uterus present as well-defined round or oval low-signal intensity masses on T2-weighted MR images. They are characterized by expansive growth but do not infiltrate surrounding structures and therefore distort the shape of the uterus in relation to their size and location. MRI performed in three orthogonal planes allows one first to accurately localize leiomyomas as submucosal, intramural, transmural (full thickness), subserosal, pedunculated, or (extrauterine) intraligamentous and second to assign them to the cervix (less than 8%), uterine corpus (anterior, posterior, lateral uterine wall), or fundus. Uterine leiomyomas can be single but usually are multiple and may reach considerable size. In a multifibroid uterus normal myometrium often represents only a minor portion of the uterine tissue (Fig. 5.12). Diffuse leiomyomatosis is a rare form where the myometrium is displaced by confluent leiomyomas [89] (Fig. 5.13).

5.3.2.3 Locations, Growth Patterns, and Imaging Characteristics

The localization of leiomyomas by imaging is of clinical importance because symptoms are related to and treatment varies based on the position of a fibroid within the uterus. Whether a submucosal leiomyoma can be resected depends on its size and ingrowth into

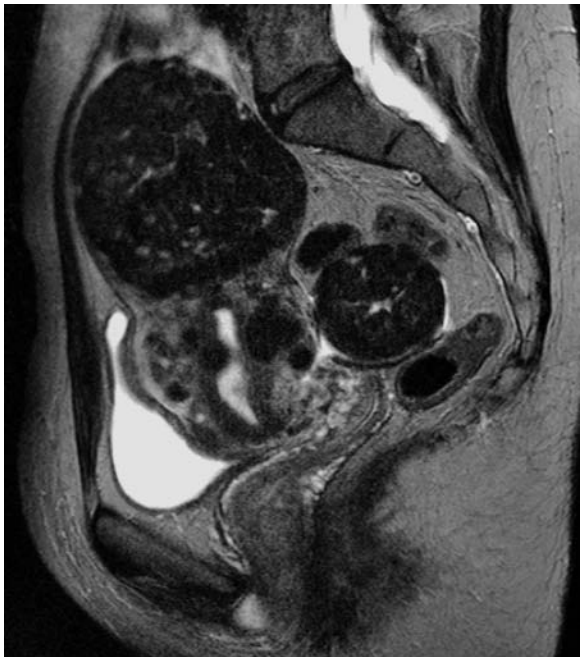


Fig. 5.12. Polyfibroid uterus – MRI appearance. T2-weighted sagittal image of a 44-year-old women shows multiple uterine leiomyoma, the largest extending subserosal from the fundus of the uterus. All leiomyomas are well marginated and show typical hypointense signal intensity with some speckled hyperintense spots. A pedunculated subserosally leiomyoma is present in the posterior cul-de-sac

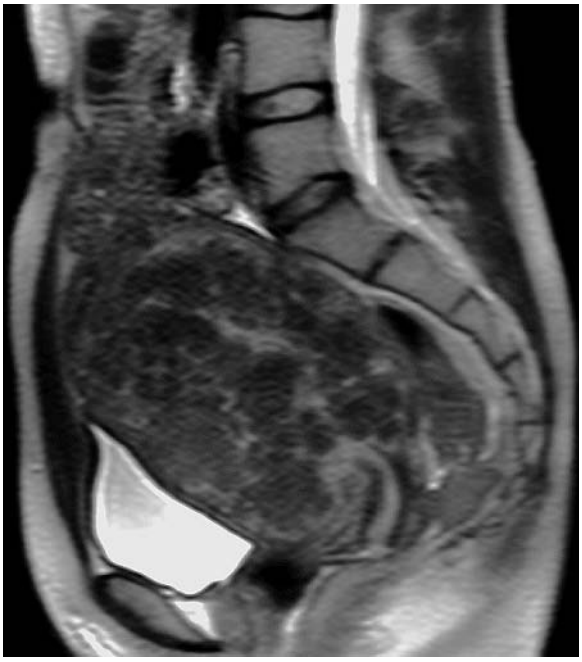


Fig. 5.13. MRI of diffuse leiomyomatosis of the uterus. T2-weighted sagittal image of a 41-year-old women shows multiple uterine leiomyoma throughout the uterine layers ranging from millimeters to several centimeters in size. The leiomyomas are partially confluent and have replaced almost the entire normal myometrium (compare also with Fig. 5.3)

the uterine wall [210]. A subserosal leiomyoma can be surgically treated by enucleation but opening and surgical reconstruction of the uterine cavity may be necessary if the leiomyoma grows transmurally [188]. Leiomyomas are characterized by expansive growth with displacement of neighboring tissue and therefore already have a mass effect when they are still small. Deformity of the uterine contour is primarily associated with submucosal and subserosal fibroids because they distend neighboring layers such as the endometrium and serosa (Fig. 5.14). In patients with a markedly enlarged uterus due to multiple fibroids, these tumors are often difficult to differentiate from extrauterine or ovarian lesions on ultrasound. The presence of a claw-like extension of myometrium surrounding the lesion and corkscrew-like flow voids at the interface between lesion and normal uterine tissue, which can be detected on T1-weighted images, less commonly on T2-weighted images, indicate uterine fibroids with a high degree of certainty [91, 171, 196, 212]. These flow voids represent the arteries arising from the uterine artery and feeding the large-caliber vascular plexus of a fibroid (Fig. 5.15). The MR imaging signs of uterine leiomyomas are summarized in Table 5.1.

5.3.2.4 Histologic Subtypes and Forms of Degeneration

Different histologic subtypes of leiomyomas exist, some of them showing characteristic features on MRI. Cellular leiomyomas, a subgroup of leiomyomas characterized by compact smooth muscle cells with little intervening collagen, exhibit a homogenously high signal intensity on T2-weighted images (Fig. 5.16). They are isointense to surrounding myometrium on T1-weighted images and tend to enhance fairly homogenously after gadolinium administration [216]. Lipoleiomyoma is a rare type of leiomyoma which displays a signal intensity similar to subcutaneous fat on all pulse sequences due to the presence of various amounts of fat cells. Chemical shift imaging or spectral fat suppression may be useful to determine the fatty nature of these leiomyomas [201]. While MRI can dis-

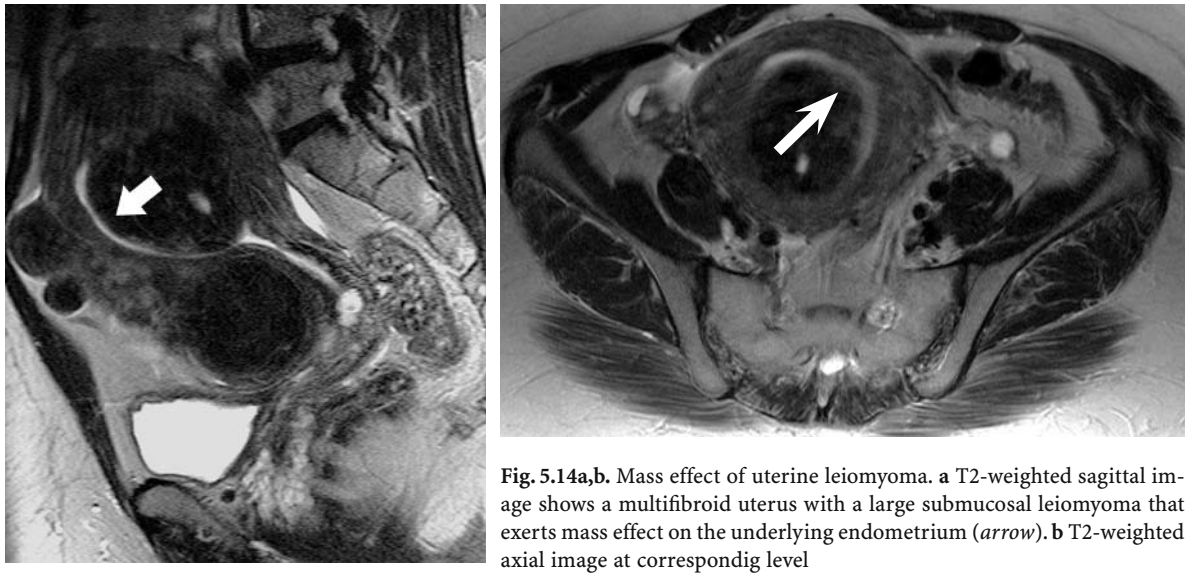


Fig. 5.14a,b. Mass effect of uterine leiomyoma. **a** T2-weighted sagittal image shows a multifibroid uterus with a large submucosal leiomyoma that exerts mass effect on the underlying endometrium (*arrow*). **b** T2-weighted axial image at correspondig level

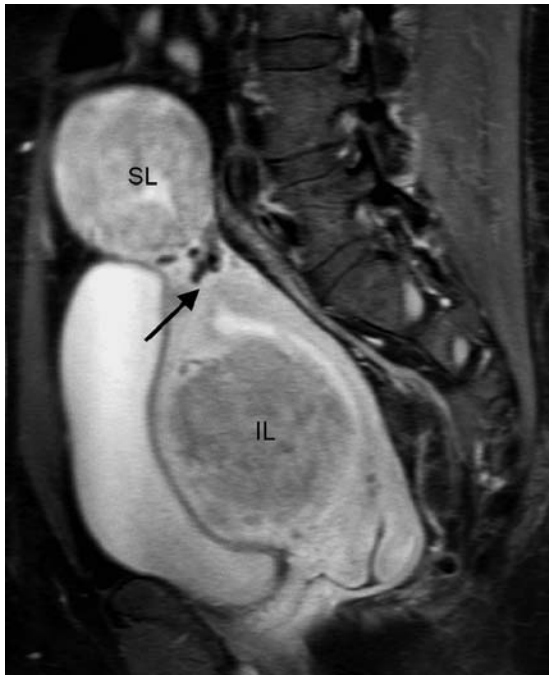


Fig. 5.15. Bridging vascular sign in a pedunculated leiomyoma. T1-weighted contrast-enhanced fat-suppressed sagittal image depicts a large pedunculated subserosal leiomyoma originating from the uterine fundus. Flow-voids are seen within the vessel stalk (*arrow*). A second intramural leiomyoma in the anterior wall is seen displacing the endometrial stripe. (Reproduced with permission from [223])

Table 5.1. MRI criteria for leiomyoma

Location	• Corpus, fundus, less often cervical or within uterine ligaments, subserosal, intramural, transmural, submucous, pedunculated, in statu nascendi
Morphology	• Spherical, sharply marginated, pseudocapsule may be present, mass effect even if small, deforming the uterine outline and/or cavity may be singular but often numerous • Size range from 0.5 cm - > 20 cm • Claw-like extension of myometrium surrounding the lesion
Appearance on T1	• Isointense to the myometrium • Peripheral hypointense rim indicates calcification • Hyperintense areas related to hemorrhage • Peripheral high SI rim or homogenous high SI indicates hemorrhagic infarction
Appearance on T2	• Variable, in general hypointense mass relative to myometrium but different SI seen in individual leiomyomas • Homogenously high SI often seen in cellular leiomyomas • High SI rim represents dilated lymphatics in large leiomyoma
Appearance on Gd-enhanced T1	• Can appear hypo-, iso- and hyperintense relative to myometrium Hypervascularity often seen in cellular leiomyomas • Pseudocapsule more prominent • Absence of enhancement seen in partially or completely infarcted leiomyoma (bridging-vascular-sign)
Additional findings	• Flow voids in the periphery (best seen on T1-weighted images) indicate the perifibroid plexus vessels • A vessel stalk may be seen in pedunculated leiomyomas

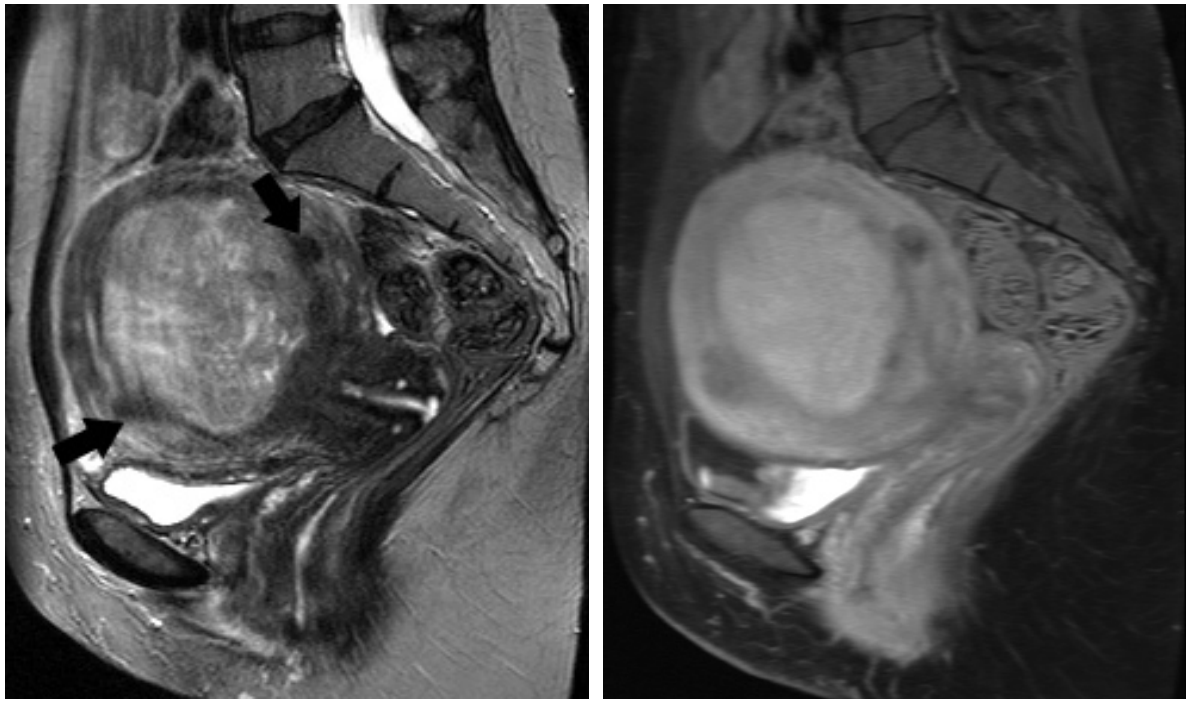
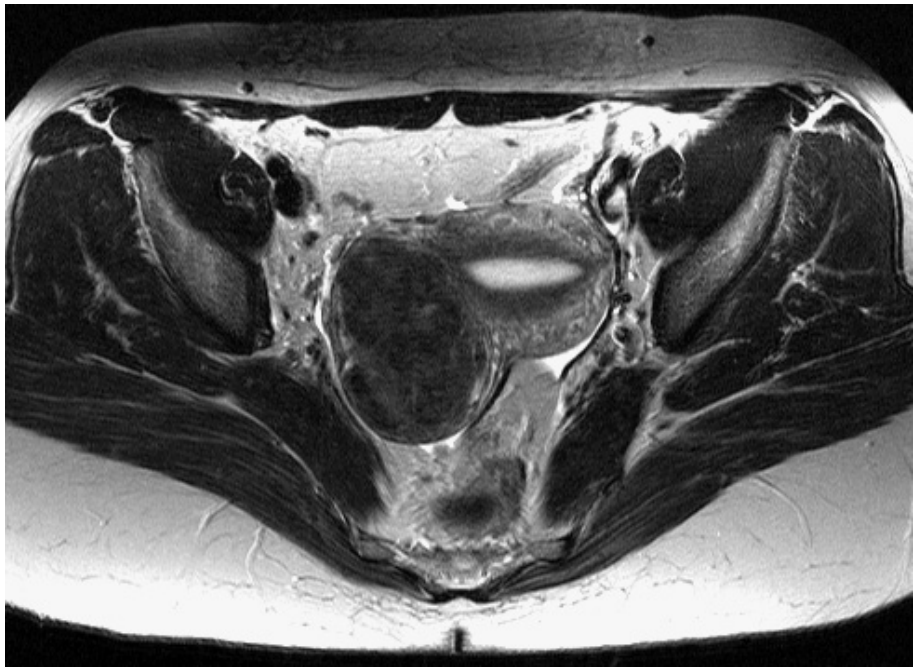


Fig. 5.16a,b. MRI of cellular leiomyoma. **a** T2-weighted sagittal image of the uterus demonstrating a large intramural cellular leiomyoma with homogenous high signal intensity compared to surrounding myometrium. Two small intramural leiomyoma show the typical low intensity signal (*arrows*). **b** T1-weighted contrast-enhanced fat-suppressed sagittal image showing marked enhancement of the intramural cellular leiomyoma which appears hyperintense compared to surrounding myometrium

tinguish among the different subtypes in only 69% of all cases, the method is highly sensitive and specific in identifying simple fibroids without any major degenerative changes, fibroids having undergone hemorrhagic infarction, and fibroids with cystic degenerative changes [169]. Degeneration of uterine leiomyomas is common and is attributed to an inadequate blood supply. It is a sudden event in case of hemorrhagic degeneration or degenerative changes may develop gradually when a tumor outgrows its blood supply.

The typical MRI appearance of a smoothly marginated tumor with a nearly homogeneous low signal intensity relative to surrounding myometrium on T2-weighted images and intermediate signal on T1-weighted images (Fig. 5.17) is attributable to hyalinization [129]. Hyaline degeneration is the predominant form of degeneration and is present in about 60% of all leiomyomas. It is characterized by the accumulation of high-protein eosinophilic substrate in the extracellular spaces between strands of muscle cells. Other types of degeneration that can be differentiated are cystic, myxoid, and hemorrhagic (red) degeneration. Cystic degeneration is characterized by the presence of clearly delineated cystic lesions with a signal intensity isointense to fluid on T1- and T2-weighted images. Myxoid degeneration is seen as intralesional areas of very high signal intensity on T2-weighted images. These portions represent viable tissue and are of intermediate to low signal on T1-weighted images and typically show enhancement after contrast medium administration (Fig. 5.18). Histology demonstrates gelatinous portions containing hyaluronic mucopolysaccharides. Hemorrhagic or red degeneration is more common during pregnancy or in women on gestagen therapy. It is attributed to sudden infarction of fibroid tissue with secondary intralesional hemorrhage [59]. MRI shows a lesion with an increased internal signal and a low-signal-intensity margin on T2-weighted images while T1-weighted images depict a lesion with a heterogeneous high signal that varies with the amount of blood degradation products present and is often confined to the margin (Fig. 5.19) [86]. Hemorrhagic fibroids typically show no enhancement after contrast medium administration. MRI confirms the diagnosis of acute hemorrhagic degeneration in conjunction with the clinical symptoms comprising acute pain, subfebrile temperature, and leukocytosis [57, 86].



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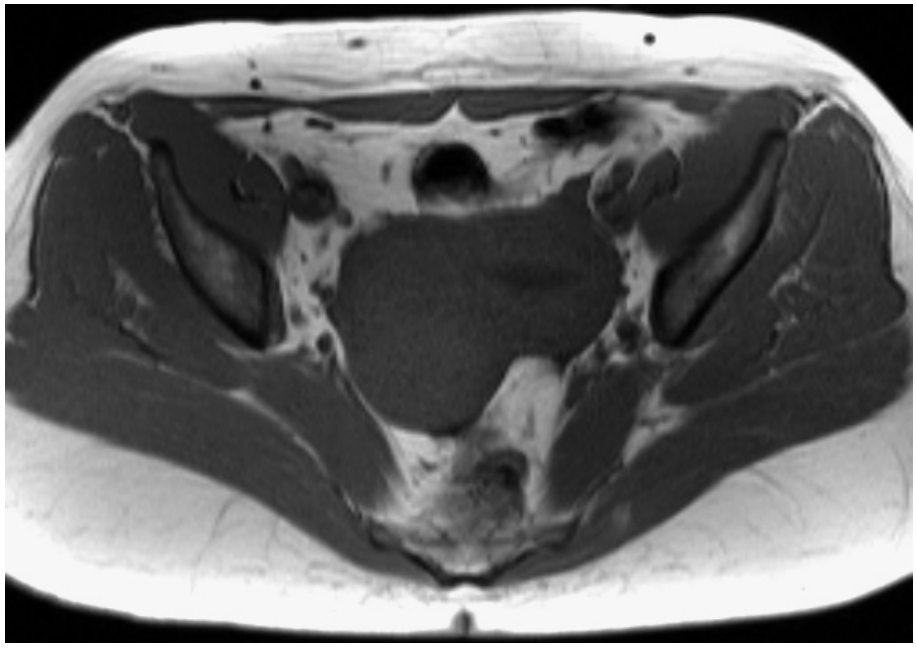
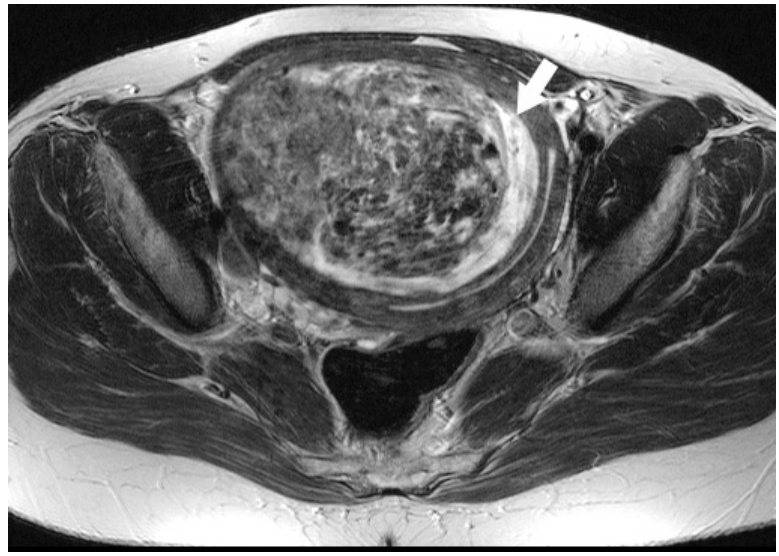


b

Fig. 5.17a,b. Signal intensity characteristics of leiomyoma. **a** T2-weighted transaxial image of the uterus (secretory phase of menstrual cycle) showing a subserosal leiomyoma with typical low signal intensity compared to adjacent myometrium. Note the bright signal of the endometrium and intermediate signal intensity of the junctional zone. **b** Corresponding T1-weighted transaxial image of the uterus showing intermediate signal intensity of the leiomyoma which can hardly be differentiated from the adjacent myometrium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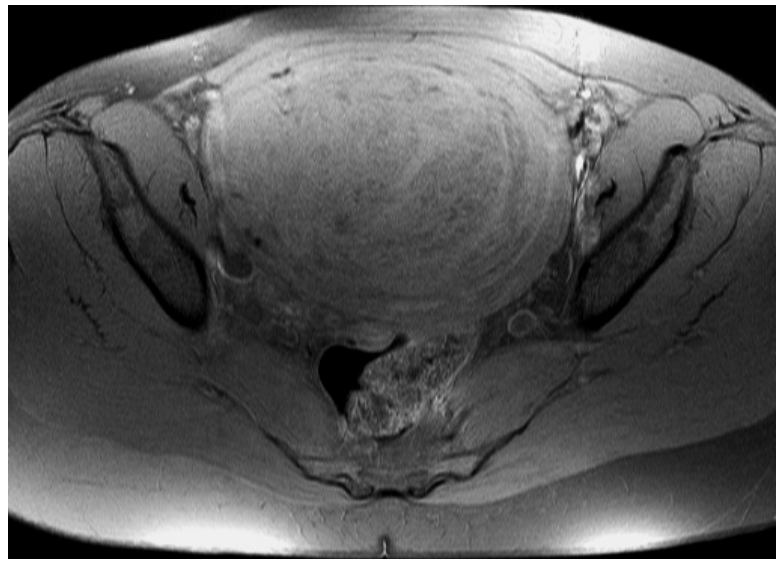
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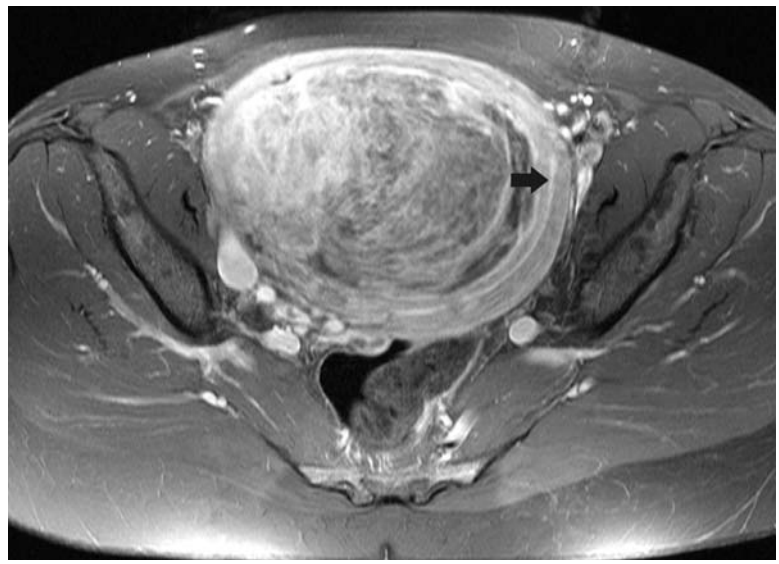
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Fig. 5.18a–c. a,b MRI of myxoid leiomyoma. **a** T2-weighted transaxial image of the uterus showing also heterogenous signal intensity of the leiomyoma and a c-shaped area at the left border of the leiomyoma (*arrow*) of high signal intensity corresponding to myxoid degeneration. Note high signal intensity stripe of the endometrium is displaced laterally. **b** On the corresponding T1-weighted fat suppressed transaxial image the whole leiomyoma has a heterogenous intermediate signal intensity and the c-shaped area shows no low signal as expexted if liquification had occured. **c** Contrast-enhanced T1-weighted fat suppressed transaxial image shows heterogenous enhancement of the leiomyoma including septations of myxoid tissue, Note enhancement of endometrial stripe (*arrow*)

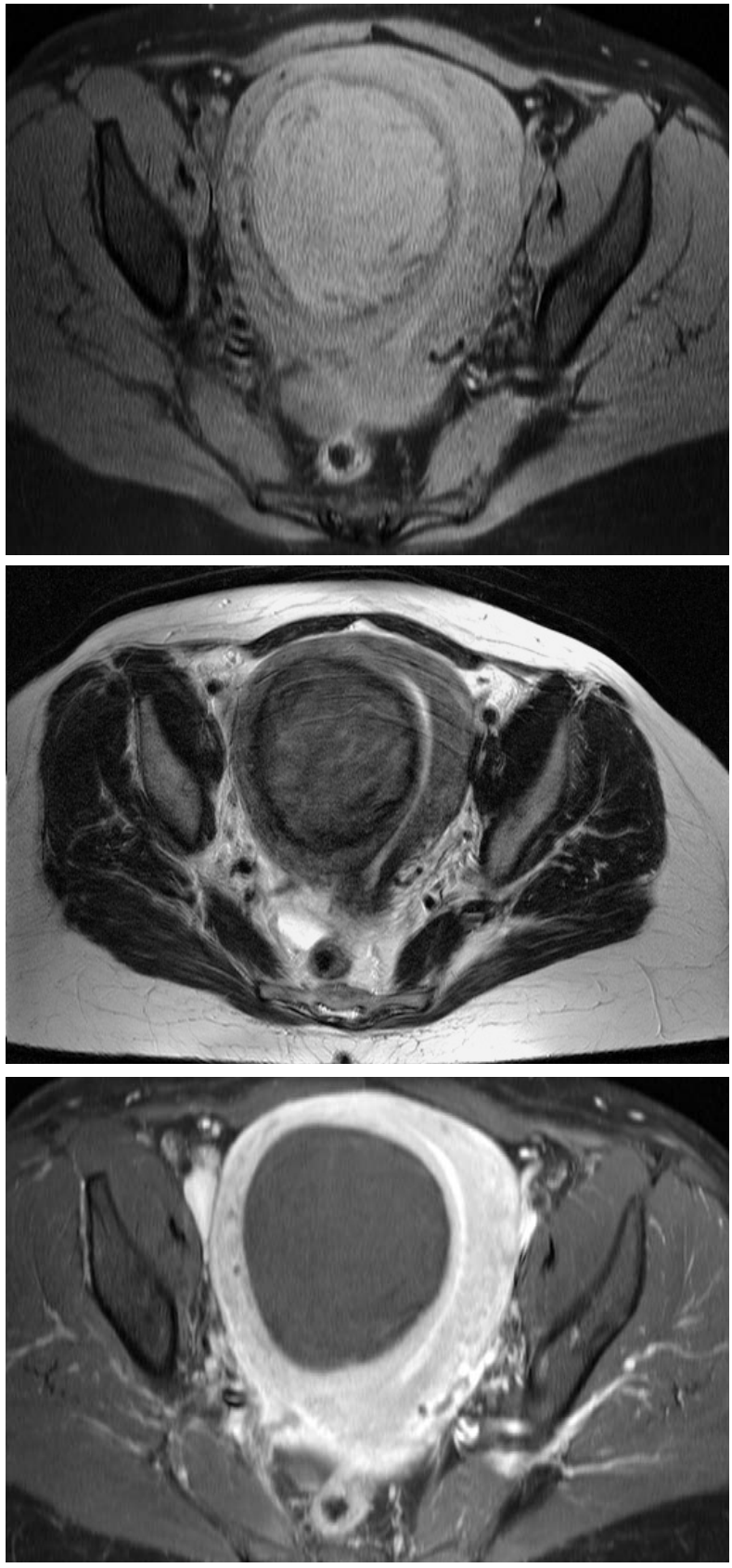


Fig. 5.19a–b. MRI of spontaneously infarcted leiomyoma. **a** T1-weighted fat-suppressed transaxial image of a spontaneously infarcted submucosal leiomyoma. The central portion shows an slightly hyperintense signal intensity compared to the surrounding myometrium. **b** T2-weighted transaxial image of a spontaneous infarcted submucosal leiomyoma. The central portion shows a signal intensity isointense to the myometrium while a marked hypointense rim is seen which corresponds to blood degradation products (hemosiderin) after hemorrhagic infarction. c Contrast-enhanced T1-weighted fat-suppressed transaxial image confirms infarction of the leiomyoma while the surrounding myometrium is well perfused(Reproduced with permission from [223])

MRI is methodologically limited in that it does not reliably show intralesional calcifications, which are frequently identified on conventional radiographs or CT scans by their popcorn-like appearance [169]. Occasionally, calcifications take the form of a peripheral rim after hemorrhagic infarction and can be identified on T1-weighted MR images (Fig. 5.20).

5.3.2.5 Differential Diagnosis

In evaluating lesions in close topographic relationship to the uterus, the examiner must consider ovarian masses in the differential diagnosis. If it is not possible to definitely assign the lesion to the uterus, an intraligamentous or ovarian fibroid may be present if the lesion shows homogeneous low signal intensity on T2-weighted images and an intermediate signal on T1-weighted images relative to the signal intensity of the myometrium of the uterus. However, an inhomogeneous intermediate, or high signal relative to the myometrium may indicate both a fibroid with degenerative changes or an extrauterine benign or malignant tumor.

Myometrial contractions can mimic submucosal leiomyomas or focal adenomyosis [193]. Uterine contractions involve the endo- and myometrium but spare the outer uterine contour (Fig. 5.21). They are characterized by band- or stick-like low-signal-intensity areas on T2-weighted images [116]. These signal changes are transient and changing appearances can be noted on sequential images obtained with a delay of 30–45 min [193, 194].

Endometrial polyps, seen most frequently in perimenopausal and postmenopausal women, are usually asymptomatic but may cause uterine bleeding, especially in postmenopausal women [33]. In 20% of the cases polyps are multiple. They can be broad-based or pedunculated and may occur in conjunction with endometrial hyperplasia. On T2-weighted images a central fibrous core or intratumoral cysts may be visible [55]. On T1-weighted images endometrial polyps show an intermediate signal while they exhibit a slightly hypointense or isointense signal intensity relative to the endometrium on T2-weighted images and present as localized endometrial thickening (Fig. 5.22). Small polyps enhance and become more conspicuous after gadolinium administration, especially on early enhanced scans while large polyps exhibit a heterogenous enhancement pattern [55, 67]. Submucosal leiomyomas are best distinguished from endometrial polyps by their rather spherical shape, their obvious connection to the myometrium, and lower signal intensity on T2-weighted images.

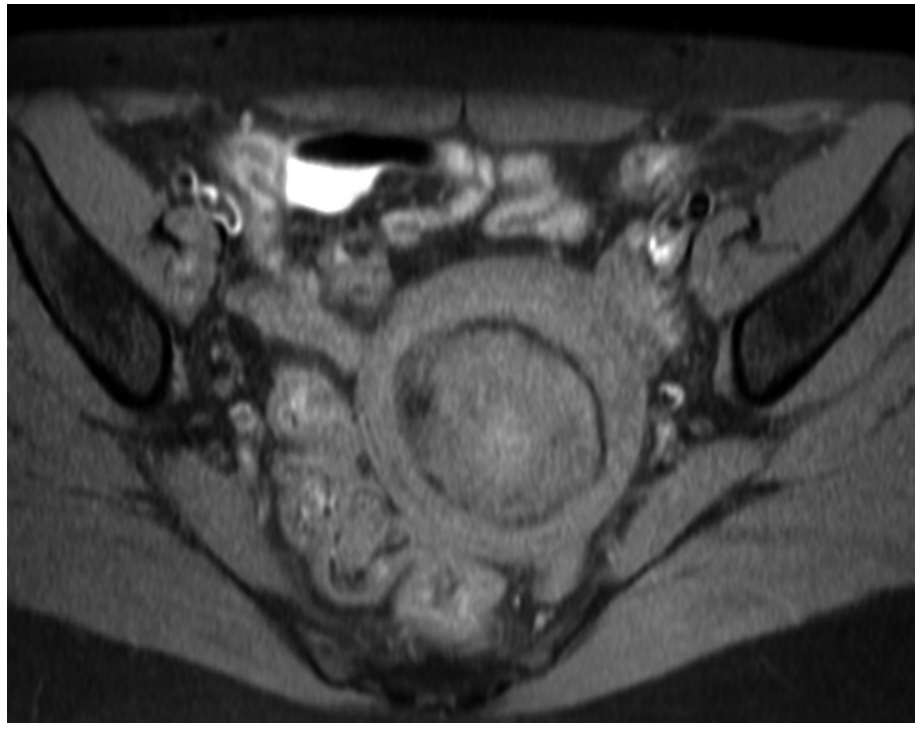


Fig. 5.20. MRI of rim calcification of a leiomyoma. T1-weighted fat-suppressed transaxial image showing a leiomyoma with a discontinuous, markedly hypointense rim corresponding to asymmetrical calcification

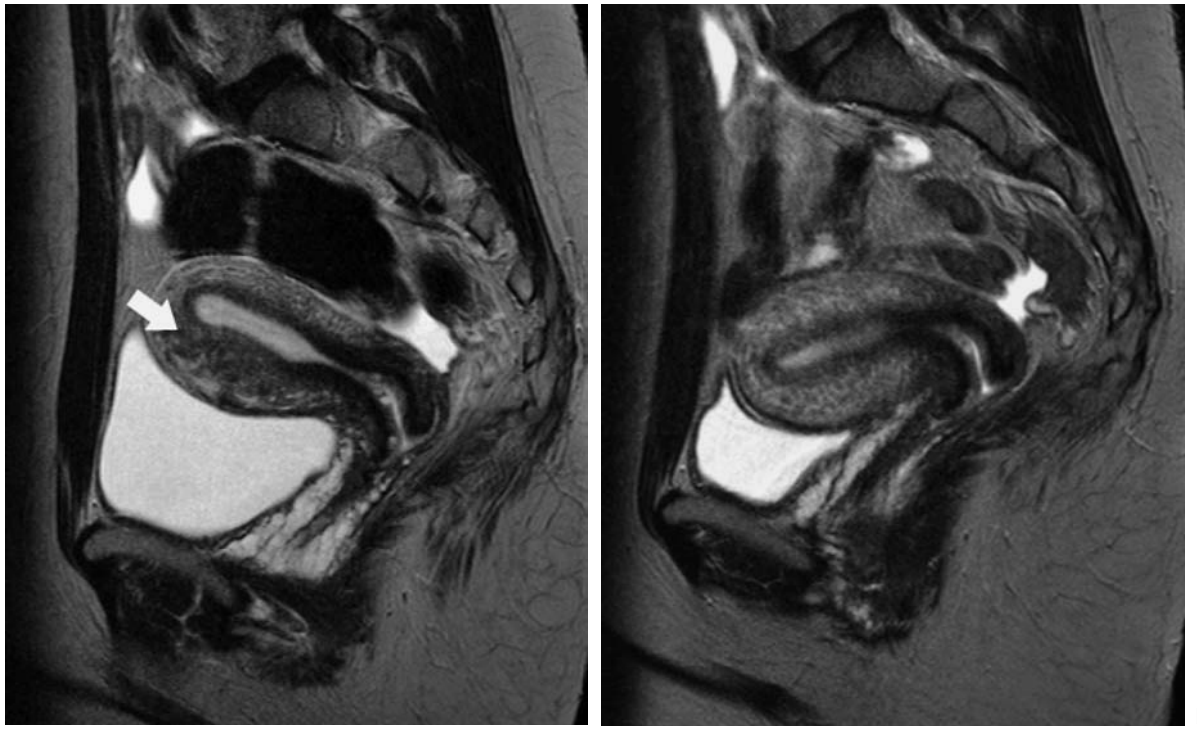


Fig. 5.21a,b. Transient uterine contraction. **a** T2-weighted sagittal image of the uterus depicting a broadening of the inner myometrium of the anterior uterine wall with bulging into the uterine cavity (*arrow*). **b** T2-weighted sagittal image of the uterus obtained 5 min before (**a**) shows absence of any structural abnormality, a finding consistent with myometrial contraction

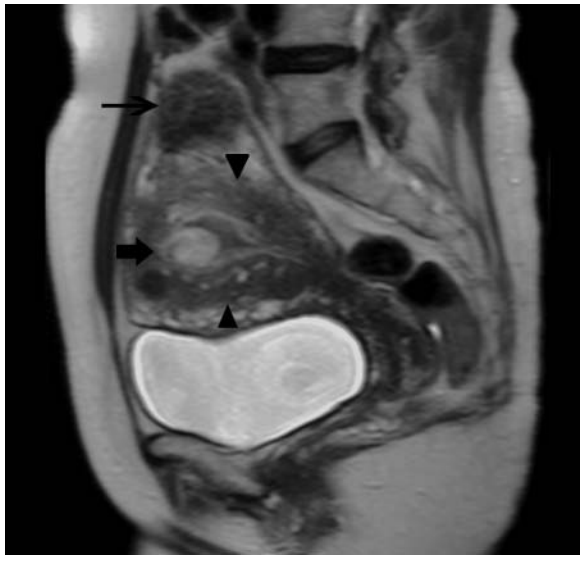


Fig. 5.22. Leiomyoma, diffuse adenomyosis and endometrial polyp on MRI. T2-weighted sagittal image of a patient depicts diffuse adenomyosis (*arrowheads*) with symmetrical broadening of the junctional zone. An endometrial polyp exhibiting similar high signal intensity as the endometrium can be clearly identified within the uterine cavity (*short arrow*). A fibroid is present in the fundus *(long arrow*)

Leiomyosarcomas of the uterus are rare with a frequency of incidentally discovered tumors of 1:2000 while large series of hysterectomy specimen quote a frequency of 2–5:1000 [3, 149]. It is felt that leiomyosarcomas arise de novo and may be unrelated to benign leiomyomas [107]. They are predominantly observed in older women (6th decade of life) as compared to women with leiomyoma (4th decade of life) [149]. While rapid growth is not an indicator of malignancy in premenopausal women, it is always suspicious in postmenopausal women although not specific [130, 137]. The imaging appearance does not enable reliable differentiation of leiomyosarcoma from benign leiomyoma [73, 137, 169, 190]. Besides frank signs of invasiveness or metastatic disease, an irregular contour, inhomogeneous appearance with pockets of high signal intensity on T2, as well as hemorrhagic changes with high signal intensity on T1 have been proposed to suggest a leiomyosarcoma rather than a leiomyoma [54, 138, 165, 169]. Recently, early enhancement on dynamic scans after administration of contrast medium together with serum determination of LDH and its isoenzymes was reported to be highly sensitive and specific in differentiating leiomyosarcoma from degenerated leiomyoma [54].

5.3.2.6 MR Appearance of Uterine Adenomyosis

Adenomyosis of the uterus is diagnosed on T2-weighted images where it is characterized by ill-defined low-signal-intensity areas representing diffuse or focal broadening of the junctional zone as a result of smooth muscle hyperplasia associated with heterotopic endometrial glands [132, 156]. A junctional zone thickness of ≥ 12 mm (Fig. 5.23) is the threshold for which a high degree of accuracy in the diagnosis of adenomyosis has been reported [79, 158]. Adenomyosis can be excluded if the junctional zone thickness is 8 mm or less [156]. Bright foci and cyst-like inclusions may be seen on T2-weighted images in up to 50% of patients and represent heterotopic endometrial glands, cystic dilatations, or hemorrhagic foci [156, 195]. Corresponding high signal on T1-weighted images is less frequently observed but highly suggestive of adenomyosis (Fig. 5.24). Additionally, striations of high signal intensity extending from the endometrium into the myometrium as a result of direct invasion of the myometrium may be seen and result in pseudo-widening of the endometrium [157]. These high-signal-intensity changes associated with adenomyosis may fluctuate during the menstrual cycle. The MR imaging signs of adenomyosis are summarized in Table 5.2.

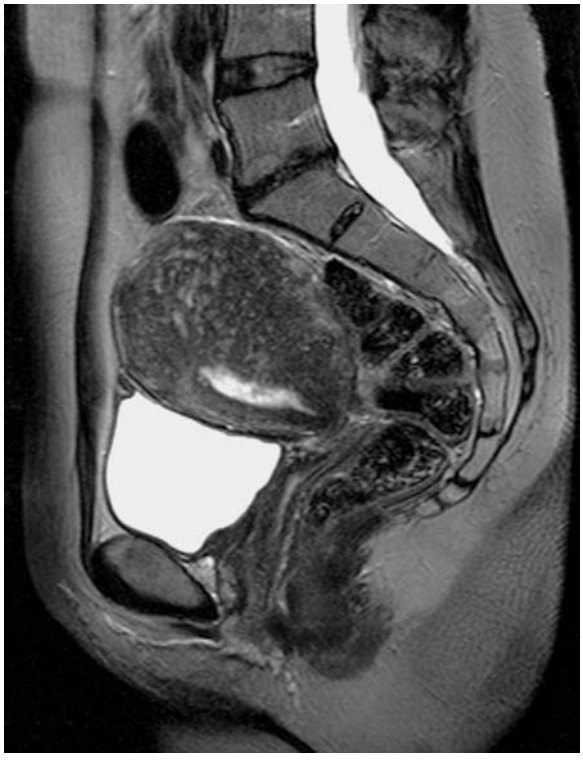
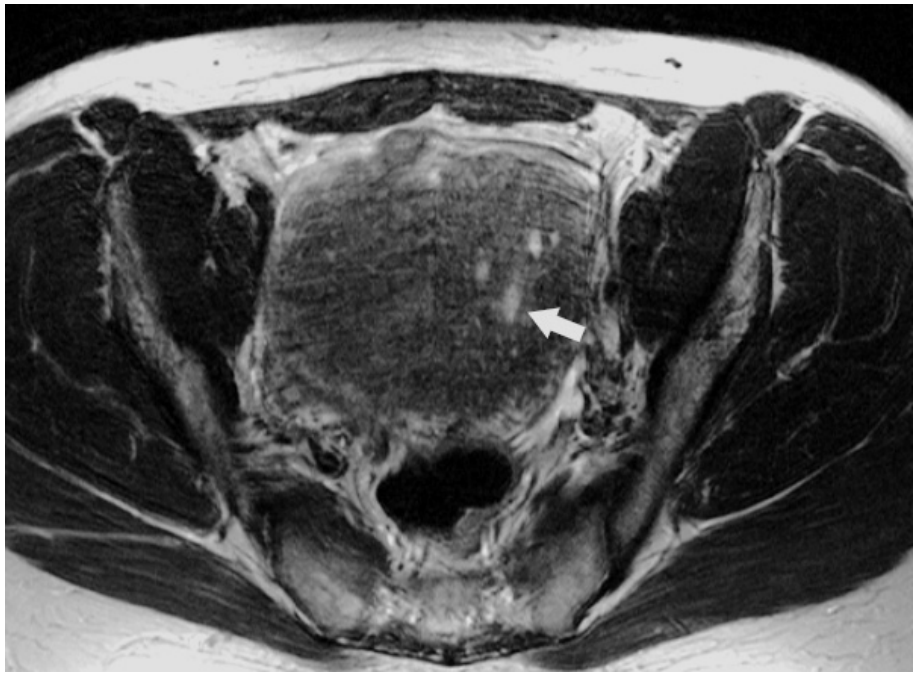


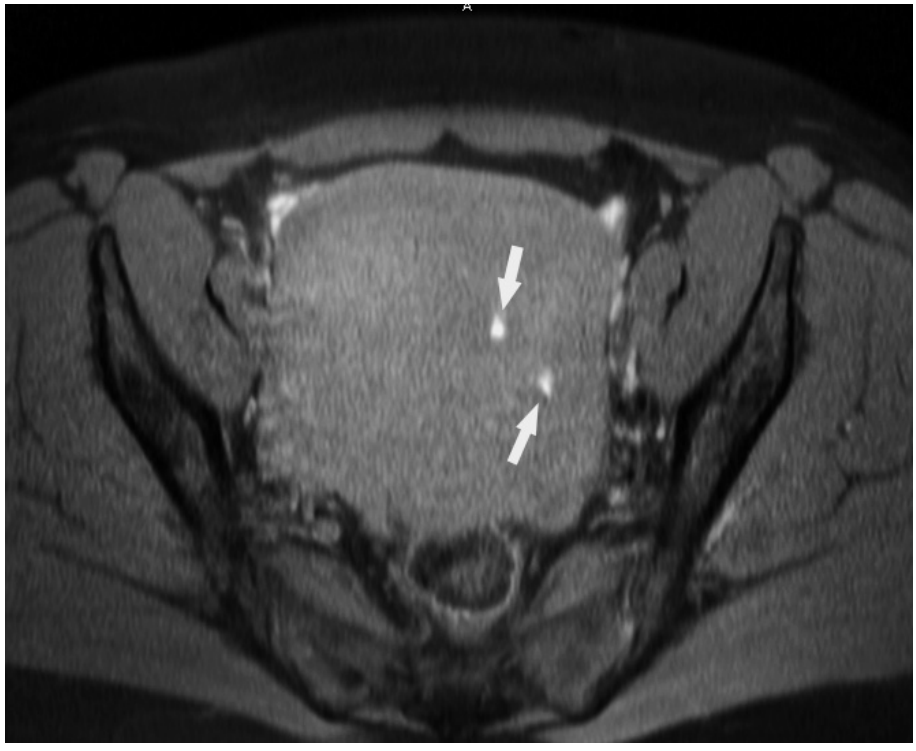
Fig. 5.23. Focal adenomyosis of the uterus. T2-weighted sagittal image of a patient with focal adenomyosis of the uterus. There is enlargement with only mild deformity of the uterus. The fundus and posterior uterine wall is thickened due to marked broadening of the junctional zone. Hyperintense foci are seen within the lesion. (Reproduced with permission from [223])

Table 5.2. MRI criteria for adenomyosis

Location	• Focal or diffuse widening of junctional zone (JZ) > 12 mm • More often found in the posterior uterine wall • Not seen in the cervix • Seldom seen as focal lesion without contact to JZ (adenomyoma)
Morphology	• Either diffusely involving the uterus or presenting as a lesion with ill-defined margins blending with the surrounding myometrium • Poor definition of endomyometrial junction • If focal, may be globular, elliptical but usually not round, spherical • Significant mass effect missing, even if large lesion present • Mild distortion of endometrium but marked enlargement of the uterus in diffuse adenomyosis • Adenomyoma may rarely present as round lesion located away from JZ • Lesion may include large cystic areas (cystic adenomyosis)
Appearance on T1	• Mostly isointense to the myometrium • May show hyperintense foci corresponding to small areas of hemorrhage
Appearance on T2	• Low SI uterine lesion with or without punctuate high SI foci scattered throughout the lesion or high SI linear striations extending from the edometrium that may lead to a pseudowidening of the endometrium • High SI (micro) cysts may be seen (< 5 mm) • Rarely large cystic spaces within a lesion (cystic adenomyosis)
Appearance on Gd-enhanced T1	• Can appear hypo-, iso- and hyperintense relative to myometrium • Perfusion abnormalities may be seen on dynamic contrast-enhanced MRI
Additional findings	• No pseudocapsule • Adenomyosis frequently seen in combination with findings of endometriosis



a



b

Fig. 5.24a,b. MRI of diffuse adenomyosis of the uterus. **a** T2-weighted transaxial image of a patient with diffuse adenomyosis of the uterus. The uterine wall is thickened, there is poor definition of the endomyometrial junction and the junctional zones blend with the myometrium. No focal mass is present. Cyst-like inclusions of hyperintense signal intensity are present (*arrow*). **b** Corresponding fat-suppressed T1-weighted transaxial image showing hyperintense spots within the myometrium indicating fresh blood related to the dislocated endometrial glands (*arrows*)

5.3.2.7 Locations, Growth Patterns, and Imaging Characteristics

Uterine adenomyosis is found more often in the posterior than in the anterior wall of the uterus and the fundus [22]. Adenomyosis does not involve the uterine cervix. A focal type can be differentiated from a diffuse type of thickening of the junctional zone. Diffuse adenomyosis (Fig. 5.25) may lead to a markedly enlarged uterus with a surprisingly small or disproportional mass effect on the uterine contour and cavity. Focal adenomyosis (Fig. 5.26) manifests as an oval or round lesion which leads to thickening of the uterine wall but differs from leiomyoma in that there is only little distortion of the uterine cavity or serosal surface. The lesion shows poorly defined margins and blends with surrounding myometrium. It lacks the pseudocapsule that may be seen with uterine leiomyoma. Signal voids at the periphery of the lesion are rare in focal adenomyosis [22]. Gadolinium-enhanced T1-weighted imaging does not increase the accuracy in diagnosing adenomyosis of the uterus although perfusion abnormalities may be seen [67]. Unusual growth patterns include adenomyoma of the uterus which represents a localized form that manifests as a myometrial or subserosal mass without a direct connection to the junctional zone [50, 191]. Another rare variant is cystic adenomyosis which is thought to result from extensive hemorrhage within adenomyotic implants, leading to a well circumscribed cystic myometrial lesion which may show different stages of blood product degradation such as a low intensity rim on T2-weighted images corresponding to hemosiderin and areas of high signal intensity on T1-weighted images representing fresh blood [157, 191, 199]. Treatment of adenomyosis by GnRH agonists may also alter its appearance on MR imaging and a decrease in junctional zone thickness and a better lesion demarcation may be observed [71].

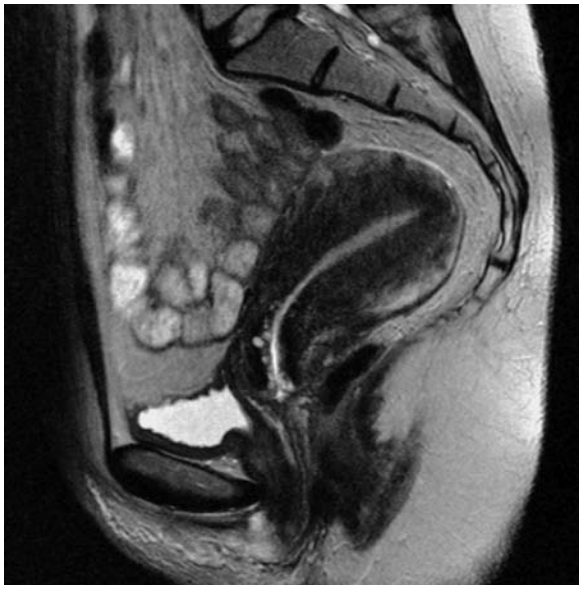


Fig. 5.25. MRI of diffuse adenomyosis of the uterus. T2-weighted sagittal image of the uterus. A broadened junctional zone (> 12 mm) is seen with poor definition of the endomyometrial junction. The junctional zone blends with the myometrium

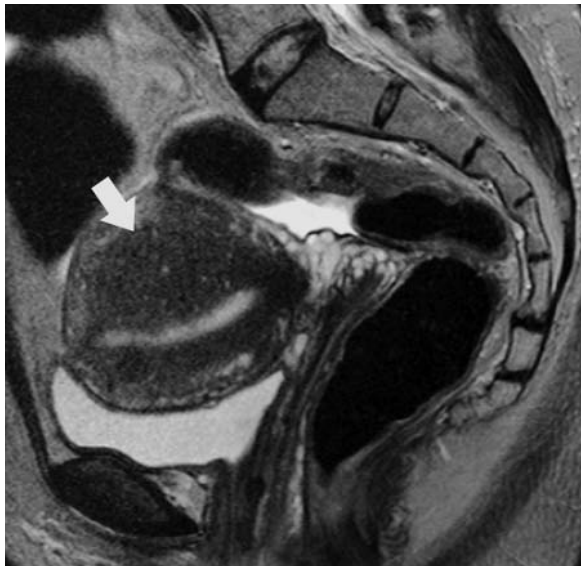


Fig. 5.26. MRI of focal adenomyosis of the uterus. T2-weighted sagittal image of the uterus. The posterior wall of the uterus is thickened and a focally broadened junctional zone with hyperintense foci appearing as a globular lesion is seen (*arrow*). The uterus is enlarged but no mass effect is seen

5.3.2.8 Differential Diagnosis

Leiomyomas of the uterus are part of the differential diagnosis for adenomyosis and differentiation is especially important since therapeutic options differ for both entities. Imaging features that favor adenomyosis are poorly defined lesion borders, minimal mass effect, an elliptical instead of a globular shape, and high-signal-intensity spots, cysts, and striations on T2-weighted imaging. Adenomyoma and cystic adenomyosis, however, may be indistinguishable from degenerated leiomyomas at MR imaging or may resemble an aggressive uterine neoplasm [28,

191]. Myometrial contractions may also mimic focal adenomyosis but are transient phenomena.

Endometrial carcinoma can show some overlap with the imaging features associated with adenomyosis such as an irregular endomyometrial junction, high-signal-intensity linear striations on T2-weighted imaging, as well as pseudowidening of the endometrium. Contrast-enhanced MR imaging has been reported to be useful in the case of endometrial carcinoma invading adenomyosis [204]. Endometrial stroma sarcoma (ESS) must also be considered when both endometrial and myometrial involvement of an apparently infiltrative lesion with cystic changes is detected [97]. A rare differential diagnosis is an adenocarcinoma arising in adenomyosis [96, 104].

5.3.3 Computed Tomography

5.3.3.1 CT Technique

Given the availability and cost-effectiveness of ultrasound as a first-line imaging tool to diagnose benign uterine lesions and the proven benefits of MRI in delineating soft tissue masses of the uterus, little room is left for the use of CT in this setting. With the advent of multislice spiral CT (MSCT) spatial resolution has improved considerably. Current scanner technology allows the acquisition of slices as thin as 0.5 mm. The generation of isotropic voxels allows multiplanar reformations in the desired plane of interest and can aid in determining the exact location of a presumed uterine lesion with respect to surrounding tissues. However, the improvement in spatial resolution is of little benefit for the diagnosis of benign uterine conditions.

5.3.3.2 CT Appearance of Uterine Leiomyoma and Adenomyosis

While there are no specific CT features of leiomyomas, their presence may be suggested by uterine enlargement, contour deformity, and the depiction of calcifications. Calcification is the most specific sign of a leiomyoma and can be found in up to 10% of cases. Calcifications may be mottled, whorled, or streaked in appearance but can also present as a well-defined peripheral rim surrounding the leiomyoma [24]. Calcifications may be found only in one of multiple leiomyomas and may be only present in a part of a fibroid. On CT leiomyomas usually exhibit a similar density as surrounding myometrium but may show low-density areas that represent degenerative cystic changes (Fig. 5.27). CT cannot reliably identify adenomyosis of the uterus. As with uterine leiomyomas, enlargement of the uterus may be present. In adenomyosis there is enlargement while a clear mass lesion or distortion of the uterine contour is absent.

5.3.3.3 Atypical Appearances on CT and Differential Diagnosis

Leiomyomas may undergo spontaneous infarction, which presents clinically as an acute abdomen. Infarction may be related to rapid growth during pregnancy or may be due to acute torsion (Fig. 5.28)

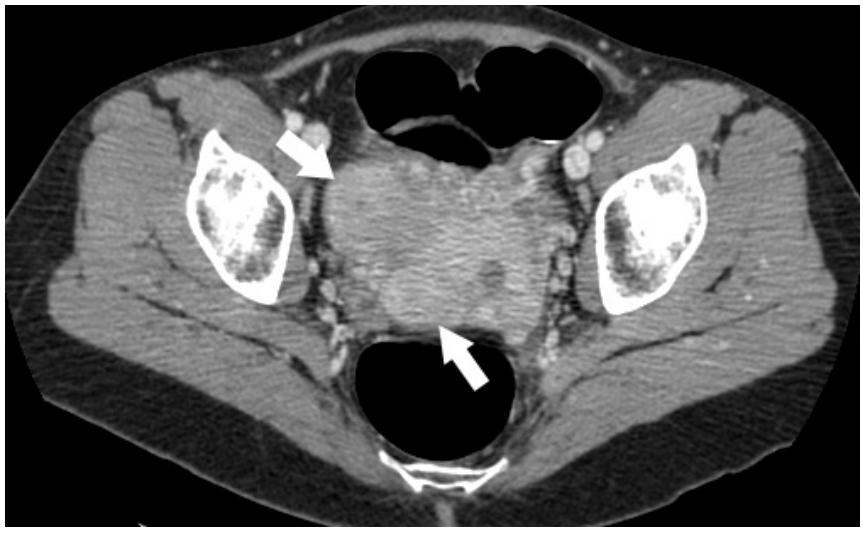
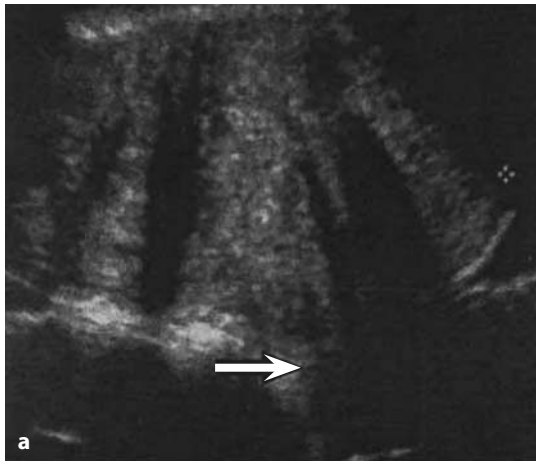
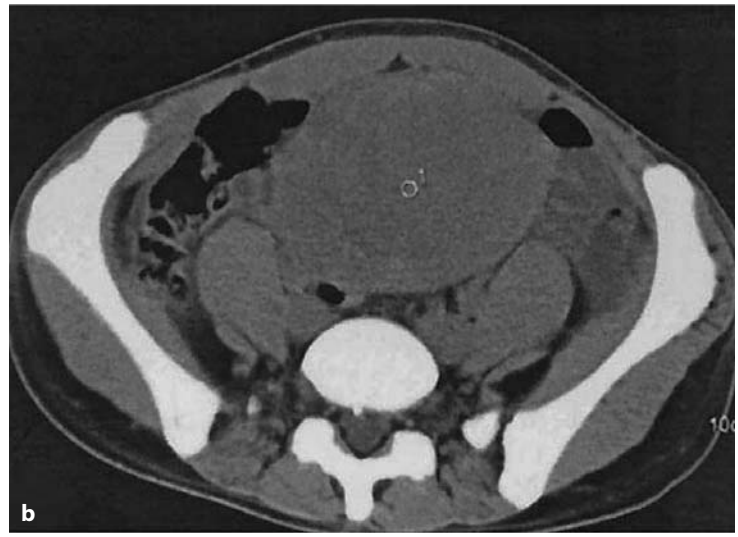
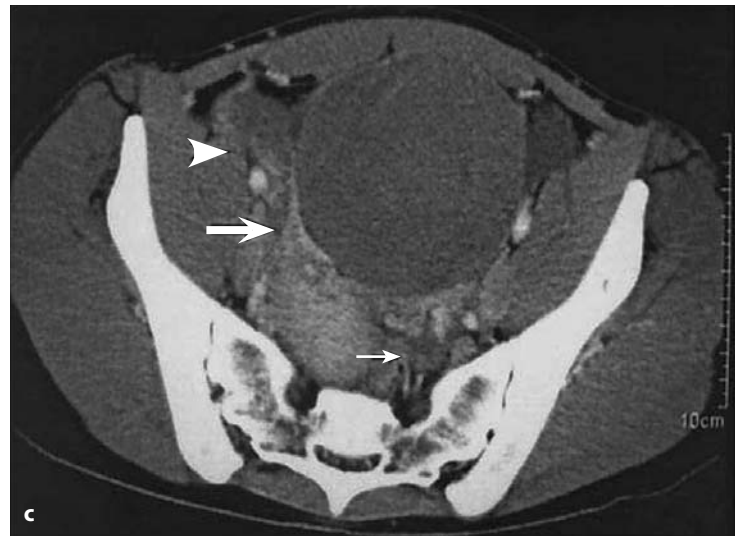


Fig. 5.27. CT of uterine leiomyomas of the uterus. Contrast-enhanced CT shows subserosal leiomyomas distorting the uterine contour (*arrows*). The fibroids show similar enhancement to adjacent myometrium







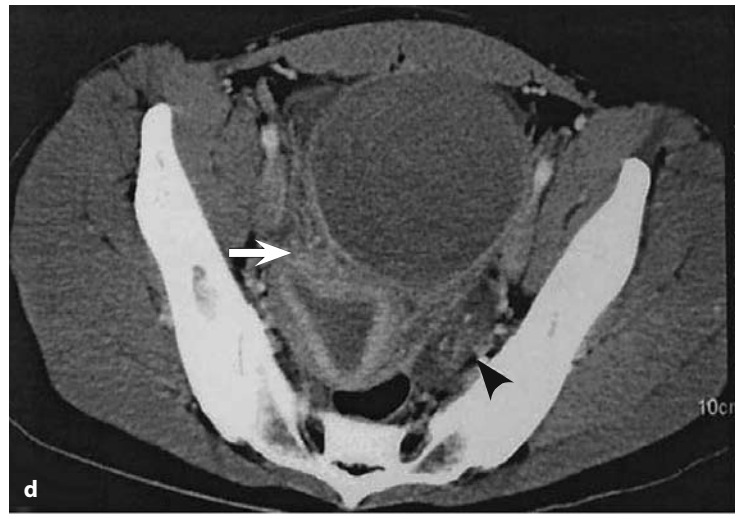


Fig. 5.28a–d. Acute torsion of a uterine leiomyoma. A 30-year-old-woman with torsion of a pedunculated subserosal leiomyoma. **a** Suprapubic US examination in the sagittal plane shows a large (13 cm in diameter), echogenic, heterogeneous mass that compresses the bladder. The uterus is displaced posteriorly (*arrow*). Shadows inside the mass are due to acoustic reflections. **b** Unenhanced CT scan shows a large, slightly heterogeneous, abdominopelvic mass (mean value 45 HU). Some linear parts have a higher value of 55 HU. **c** Contrast-enhanced CT scan shows intense rim enhancement localized against uptake of contrast medium inside tortuous vessels between the upper anterior part of the corpus uteri and the mass (*large arrow*). There is no enhancement inside the mass. The left ovary is normal and far from the mass (*arrowhead*). Note fluid inside the cul-de-sac (*small arrow*). **d** Contrast-enhanced CT scan at a level inferior to that depicted in (**c**) shows thin rim enhancement that is more intense in contact with persistent uptake of contrast medium against the anterior part of the uterus (*arrow*). No enhancement inside the mass was recorded. The endometrial cavity is normally enlarged during the second part of the menstrual cycle. The right ovary is normal (*arrowhead*). (Reproduced with permission from [224])

of a pedunculated subserosal leiomyoma [163]. On unenhanced images small areas of high attenuation indicate hemorrhagic infarction, which is confirmed on contrast-enhanced images [163]. Superinfection of leiomyomas may occur secondary to degeneration or hemorrhagic infarction if predisposing factors such as diabetes, adnexitis, or an ascending infection that can spread to leiomyomas with contact to the endometrial cavity are present. Pyomyoma develops slowly over days and weeks, particularly in patients after delivery or abortion [80]. Specific findings are hypodense areas in combination with pockets of gas within the leiomyoma. If perforation into the peritoneal cavity occurs, discontinuity of the uterine wall, intraperitoneal gas and fluid are usually present, and peritoneal enhancement is seen with peritonitis [80].

The differential diagnosis of acute torsion of a pedunculated leiomyoma includes ovarian/adnexal torsion and uterine torsion [49, 74]. The most valuable sign to diagnose acute adnexal torsion is thought to be thickening of the fallopian tube due to venous congestion and edema. Coronal and sagittal reformations from thin section contrast-enhanced MSCT also aid in identifying the ovarian vascular pedicle and confirm the ovarian origin of a pelvic tumor [105]. Uterine torsion has been reported to occur more often during pregnancy and is characterized by torsion along the corpus and cervix uteri. A whorled structure of the uterine cervix or a twisting upper vagina is seen on CT [74].

5.4 UAE for the Treatment of Leiomyoma and Adenomyosis

5.4.1 Indications

UAE is an established treatment for symptomatic fibroids. The gynecologist and interventional radiologist should closely cooperate in establishing the indication for fibroid embolization and carefully weigh the indications and contraindications in light of the range of therapeutic options available for the individual patient [53, 66]. UAE must not be performed without careful pre-interventional diagnostic workup of the patient's symptoms by the gynecologist. UAE is an alternative therapeutic option only in patients with symptomatic leiomyoma who would otherwise undergo surgery. The "ideal" candidate for UAE is a premenopausal woman with a symptomatic multifibroid uterus in whom surgery is indicated and who does not desire to preserve fertility and prefers a minimally invasive intervention. As a rule, both single and multiple fibroids can be treated by UAE. The number and location of the individual tumors (subserosal, intramural, transmural, submucosal) does not affect the approach, technique or outcome of UAE. Nevertheless, one must always thoroughly evaluate the clinical symptoms, imaging findings, and the patient's preferences on an individual basis to decide when UAE should be preferred to uterus-sparing surgical approaches or hysterectomy.

Embolization of subserosal pedunculated and intraligamentous fibroids is considered to be more risky because postprocedural necrosis of the tumors may cause peritoneal adhesions and decomposition of the fibroids into the free abdominal cavity. More recent studies, however, have not demonstrated a higher complication rate of UAE for subserosal pedunculated fibroids [81]. From the interventional radiologist's perspective, there is no size limit above which it becomes technically impossible to perform UAE. Early reports on higher complication rates in fibroids > 10 cm were not confirmed by later studies, which found good clinical results after embolization of large uterine leiomyomas [82, 147]. However, the patient must be aware that a markedly enlarged uterus will persist after UAE despite shrinkage of the fibroids in case of a multifibroid uterus associated with pronounced enlargement before the intervention. UAE is not indicated in patients with contraindications to angiography (clotting disorder, renal insufficiency, manifest hyperthyroidism) and in women with pelvic or urogenital infections (adnexitis, endometritis, urinary tract infection), an adnexal tumor, status post-pelvic radiotherapy, and suspected malignant tumor. An unwillingness to undergo follow-up examinations is a relative contraindication because follow-up is absolutely necessary to evaluate the success of the intervention and to identify and treat possible complications. Since data on the effect of UAE on fertility and the course of pregnancy after UAE is still inadequate, the wish to conceive is considered a contraindication to UAE, while a desire to have further children is a relative contraindication to embolization in those women in whom other therapeutic approaches (e.g. laparoscopic/abdominal leiomyoma resection) are an option [78, 92, 121, 145, 151, 183]. In addition to the gynecologic examination, a

recent cervical smear (Papanicolaou's smear) is required, and women with irregular periods (metrorrhagia) should undergo endometrial sampling before UAE. UAE for adenomyosis occurring either alone or in conjunction with uterine leiomyomas is still under investigation. Contrary to previous reports, UAE has been shown to be effective in the midterm for both scenarios [51, 76, 93, 94, 122, 141, 174].

5.4.2 Technique

UAE is performed under local anesthesia, which may be supplemented by sedation where required, using a transfemoral access and standard Seldinger technique. Prior to embolization, patients receive an intravenous line and a bladder catheter. A 4- or 5-F catheter sheath is placed and the internal iliac artery is probed using end-hole catheters. An abdominal aortogram or selective angiographic series of the pelvic arteries is required only in those cases where the road map of the internal iliac artery in left or right anterior oblique projection does not provide adequate information on the origin of the uterine artery. When the uterine artery is strong and its origin takes a straight course, it can be catheterized with the diagnostic catheter. However, coaxial advanced microcatheters should be used liberally to prevent vascular spasm, in particular when the uterine artery has a small caliber or its origin is at a right angle or twisted. The embolic agent is administered with the blood flow in a fractionated manner (free-flow embolization) once the catheter comes to lie in the horizontal segment of the uterine artery and the angiogram shows good flow. Spasm sometimes results in complete cessation of flow and should then be addressed with intra-arterial administration of nitroglycerin or tolazoline. In case of strong spasm, the interventional radiologist should first proceed to embolize the contralateral uterine artery and then try again. Particulate agents are used for UAE in treating both symptomatic uterine leiomyomas and adenomyosis. Well-documented experience is available with polyvinyl alcohol (PVA), Gelfoam, and trisacryl gelatin-coated microspheres (TGM) [69, 83, 93, 101, 120, 141, 142, 174, 178, 180]. Nonspherical particles measuring 350–750 μm and microspheres ranging in size from 500–900 μm are used. The angiographic endpoint using non-sherical PVA is stasis indicating complete occlusion of the uterine arteries while a limited embolization with sluggish antegrade flow but complete occlusion of fibroid plexus vessels is advovated when using trisaryl-gelantin microspheres [139, 180]. The level of occlusion is documented by last image hold or a final selective series. Following embolization of the contralateral side, the ipsilateral uterine artery is catheterized by formation of a Waltman loop or by simply pulling down a curved catheter such as the Rösch inferior mesenteric catheter which acts like a hook and easily enters the internal iliac artery. When confronted with a difficult anatomic situation on the ipsilateral side, it may become necessary to puncture the other groin for cross-over catherization. A controversy exists regarding the necessity of obtaining a final aortogram at the time of the intervention to exclude relevant collateral flow to the uterus (e.g. ovarian artery). If MR angiography is performed, relevant blood supply to the uterus through the ovarian artery can be identified noninvasively already before embolization [99]. The technical success rate is over 95% for primary bilateral embolization. Postprocedural management during the first 24(–48) h comprises adequate pain relief using intravenous opioid analgesics or placement of a peridural catheter and administration of nonsteroidal anti-inflammatory agents and antiemetic medication.

5.4.3 MR Imaging in the Setting of UAE and Uterus-Conserving Surgery

MR imaging prior to UAE or uterus-conserving surgery offers a comprehensive view of the pelvis without superimposed structures even in patients with a markedly enlarged polyfibroid uterus. It has been demonstrated that MRI affects patient treatment by reducing unnecessary surgery and identifying co-pathologies prior to UAE [131, 168]. MR imaging can aid in the preoperative planning for myomectomy by its ability to accurately determine the size and position of individual leiomyomas within the uterine wall and to differentiate conditions which may mimic leiomyoma both clinically and on ultrasound [212]. Preoperative classification of leiomyomas is of clinical significance since a submucosal tumor with a minor intramural component may be treated by hysteroscopic resection whereas a laparoscopic or transabdominal approach may be required in intramural or subserosal fibroids [36]. Knowing the position of a fibroid and the thickness of the surrounding myometrium helps one to minimize the risk of uterine perforation during hysteroscopic resection and inadvertent entry into the uter-

ine cavity at myomectomy, which is associated with synechia and may require endometrial repair [188]. MR imaging is also useful in monitoring the effect of GnRH therapy on leiomyomas [5, 221].

Besides its high accuracy in the diagnosis of fibroids and additional pathologies of the adnexa prior to UAE, MR imaging enables identification of tumors in which embolization is associated with a higher risk such as subserosal pedunculated fibroids (Fig. 5.15) with a narrow stalk or those which will probably not respond to embolization due to their parasitic blood supply such as intraligamentous leiomyomas. However, the ability of MR imaging to predict a successful clinical outcome based on the location, size, and signal intensity of a leiomyoma is still under investigation [20, 75, 184].Three-dimensional contrast-enhanced MR angiography can show the uterine arteries and collateral flow via enlarged ovarian arteries and may serve as a "road map" prior to embolization (Fig. 5.29).

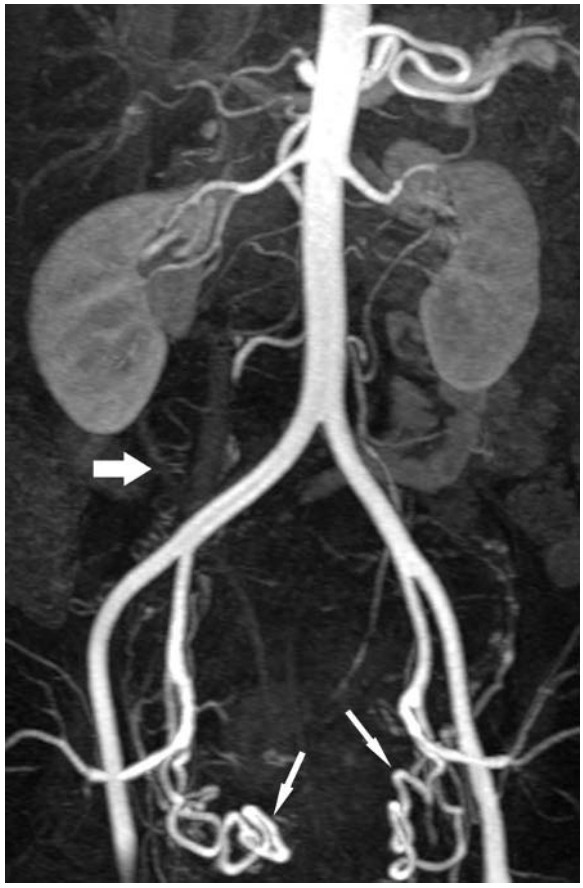


Fig. 5.29. Contrast-enhanced MRA prior to UAE. Maximum intensity projection of a T1-weighted contrast-enhanced MR angiography depicts the uterine arteries (*long white arrows*) as well as an enlarged the right ovarian artery (*thick white arrow*)

Typical imaging features are observed after fibroid embolization (Fig. 5.30). The tumors show a homogeneous low signal intensity on T2-weighted images after UAE and high signal intensity on T1-weighted images due to hemorrhagic infarction (Fig. 5.31).

MR imaging also depicts morphologic changes such as sloughing of fibroids in contact with the uterine cavity (Fig. 5.32). The latter may be associated with vaginal discharge in patients having undergone UAE but does not require additional treatment in the majority of cases [208]. MRI also identifies side effects and complications associated with UAE such as ongoing fibroid expulsion, endometritis, and uterine necrosis [95, 197]. In cases of ongoing fibroid expulsion a dilated cervical os and leiomyoma tissue pointing towards the cervix may be observed (Fig. 5.33). Endometritis is seen in 0.5% of cases after UAE, is associated with fibroid expulsion, and usually responds well to antibiotics but may spread and result in septicemia if left untreated. At MR imaging tissue within the uterine cavity may be observed together with high-signal-intensity fluid on T2-weighted images indicating retained fluid. Punctuate foci of low signal intensity represent signal voids due to the presence of air on T1- and T2-weighted images. Contrast-enhanced MR images increase the conspicuity of intracavitary fluid collections and also depict hyperperfusion of inflamed adjacent endometrium [95]. Contrast-enhanced MRI is helpful in determining persistent perfusion of fibroids and adenomyosis after UAE. It has been demonstrated that persistent perfusion may lead to regrowth of leiomyoma tissue and recurrence of symptoms [140]. It is important to know that uterine or individual leiomyoma size reduction is not a good indicator of successful embolization since even a partially infarcted leiomyoma undergoes shrinkage while at the same time perfused areas may be present from which the tumor may regrow. The frequency of recurrence of symptoms in cases of persistent perfusion is largely unknown, but it is generally accepted among interventional radiologists that persistent perfusion of leiomyoma tissue in the setting of recurrent symptoms indicates technical failure of UAE, which may be attributable to underembolization (causes: vasospasm during UAE, inadequate choice of level of occlusion or of embolic agent) or collateral supply. Complete infarction of leiomyomas indicates technical success of UAE and is associated with long-term clinical success [140].

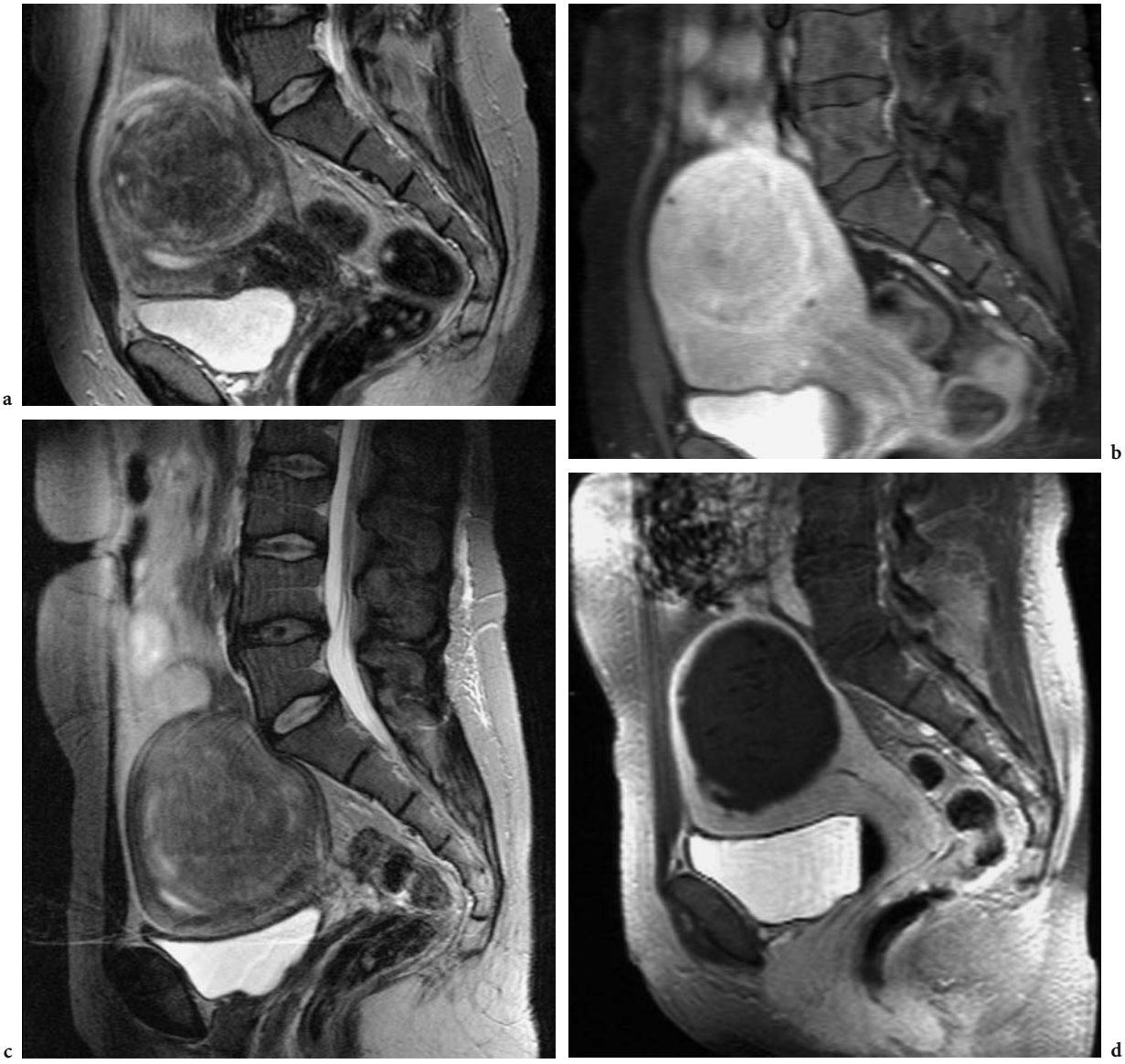


Fig. 5.30a–d. MR imaging features of leiomyoma before and after UAE. **a** T2-weighted sagittal image prior to UAE depicts an intramural leiomyoma with iso- to hypointense signal intensity compared to the adjacent myometrium of the uterus. **b** Contrast-enhanced T1-weighted fat-suppressed sagittal image prior to UAE. Strong enhancement of the uterus and leiomyoma. **c** T2-weighted sagittal image 72 h after UAE. The leiomyoma shows an increased signal intensity due to edema. **d** Contrast-enhanced T1-weighted sagittal image obtained 72 hours after UAE shows complete lack of enhancement of the leiomyoma consistent with infarction. The myometrium shows normal perfusion. (Reproduced with permission from [223])

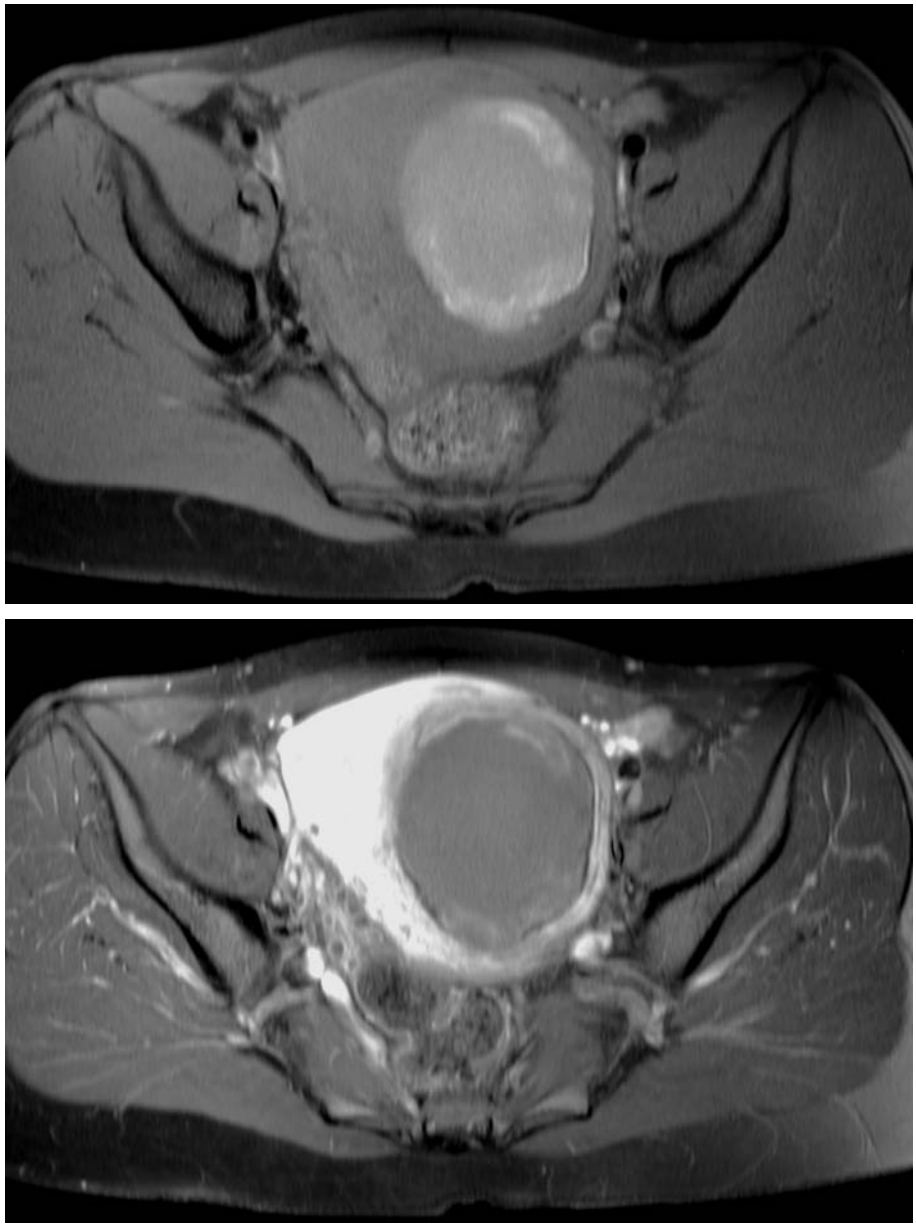


Fig. 5.31a,b. MRI of hemorrhagic leiomyoma infarction: "bag-of-blood-sign". **a** Transaxial T1-weighted fat-suppressed image obtained 3 months after UAE. Peripherally accentuated hyperintense signal intensity of the leiomyoma indicating hemorrhagic transformation of the leiomyoma ("bag-of-blood-sign"). **b** Transaxial contrast-enhanced T1-weighted fat-suppressed image obtained 3 months after UAE. Lack of enhancement of the leiomyoma consistent with infarction. (Reproduced with permission from [223])

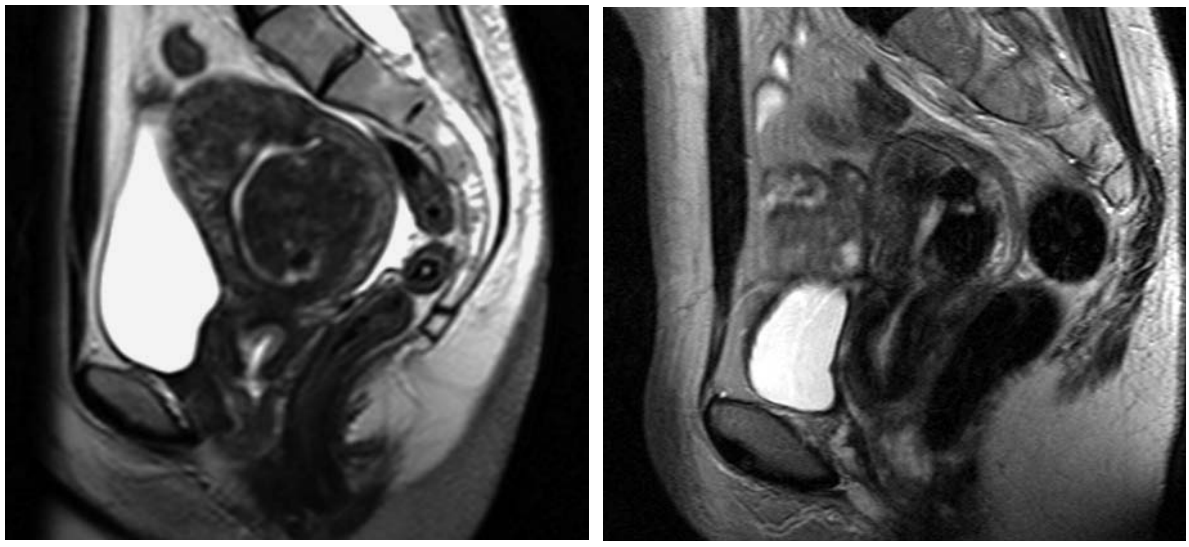


Fig. 5.32a,b. Sloughing of uterine fibroids after UAE. **a** Sagittal T2-weighted prior to UAE shows an intramural leiomyoma in the fundus and a submucosal leiomyoma in the posterior uterine wall. **b** Sagittal T2-weighted 24 months after UAE. While the patient reported marked improvement of leiomyoma-associated menorrhagia as early as 3 months after UAE, a late follow-up MRI shows marked decrease in size of the leiomyoma due to ongoing fibroid sloughing

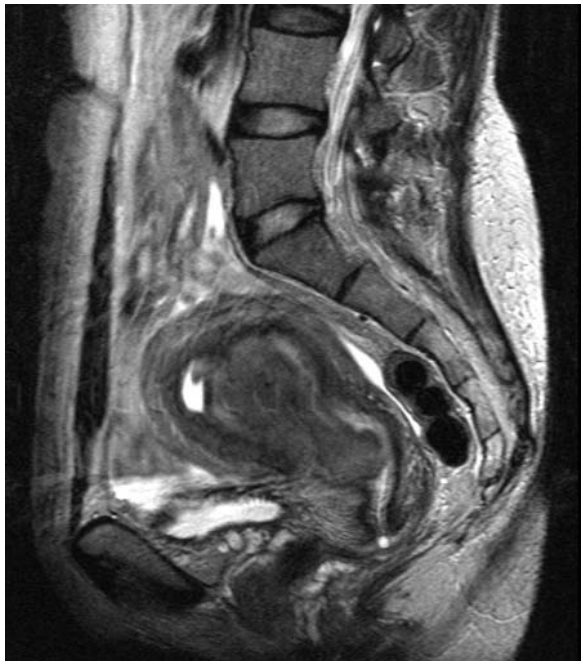


Fig. 5.33. MRI of ongoing leiomyoma expulsion. T2-weighted sagittal image of a patient 72 h after UAE. A submucosal fibroid shows the typical homogenous high signal intensity of edematous change after embolization. The leiomyoma is deformed, mainly within the uterine cavity and points towards the cervix. This finding, together with clinical signs (crampy pain), is indicative of ongoing fibroid expulsion

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