9 Adenomyosis and Ultrasound: The Role of Ultrasound and Its Impact on Understanding the Disease

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Abstract

Transvaginal sonography had a sensitivity of 80–86 %, specificity of 50–96 %, and overall accuracy of 68–86 % for diagnosing diffuse adenomyosis. These figures are poorer in the case of focal adenomyosis or if there are coexistent fibroids. Three dimensional (3D-TVS) transvaginal sonographic signs of adenomyosis are based on the evaluation of the junctional zone on the acquired volume of the uterus in order to obtain the coronal view. Three dimensional transvaginal sonography seems to be more accurate than conventional two dimensional (2D-TVS) ultrasound in detecting adenomyosis.

A strong association is found between deep infiltrating endometriosis and the presence of 2D-TVS/3D-TVS features of adenomyosis. A detailed non-invasive diagnosis of the extent of adenomyosis can facilitate the choice of safe and adequate treatment.

Keywords

Adenomyosis • Junctional zone • 3-dimensional ultrasound • 2-dimensional ultrasound • Two dimensional ultrasound • Three dimensional ultrasound • Transvaginal ultrasound • Magnetic resonance imaging • Junctional zone • Volume contrast imaging • Multi-planar view • Diffuse adenomyosis • Focal adenomyosis • Doppler flow

Introduction

Adenomyosis is a common gynaecologic disease characterized by the migration of endometrial glands and stroma from the basal layer of endometrium into the myometrium, and associated smooth muscle hyperplasia. This generates ultrasound appearance of ill-defined lesions within the myometrium. Adenomyosis may be

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present in one or more sites within the uterine wall or may involve most of the myometrium. Often adenomyosis is dispersed within the myometrium (*diffuse adenomyosis)* rather than being confined to localised lesions. On the other hand, *focal adenomyosis* is the term used to describe adenomyosis present in only one part of the myometrium. Adenomyoma is used to describe a focal lesion with additional compensatory hypertrophy of the surrounding myometrium and in rare cases it may present as a large cyst (*adenomyotic cyst* or *cystic adenomyoma*).

Detection of adenomyosis remains a diagnostic challenge. Transvaginal ultrasound and magnetic resonance imaging (MRI) have high levels of accuracy in the preoperative diagnosis of adenomyosis [1]. Several studies have illustrated that the sensitivity and specificity of two dimensional transvaginal sonography (2D-TVS) in diagnosing adenomyosis are comparable to those of MRI and/or histology ranging from 75–88 % and 67–93 % respectively [2–6]. However, compared to MRI, transvaginal ultrasound is well tolerated by patients, is repeatable, inexpensive and widely available.

The presence of adenomyosis denotes hyperplasia and hypertrophy of myocytes surrounding heterotopic endometrial tissue and can be seen on T2-weighted MRI as diffuse or focal thickening of the junctional zone (JZ). The 2D-TVS features of adenomyosis described in the literature are generally alterations of the outer myometrium. Because optimal sonographic differentiation into inner and outer myometrium is often absent, 2D-TVS transvaginal sonographic evaluation of the junctional zone, including with the use of high-frequency probes (5–10 MHz), is often difficult and imprecise. Recently, it has been observed that it is possible to visualize the junctional zone more clearly with some post-processing using coronal section of the uterus obtained with three dimensional (3D-TVS) transvaginal sonography [7–9].

Table 9.1 Summary of the ultrasound features associated with histological diagnosis of adenomyosis

	Feature
2D-TVS	
Serosal contour of the uterus	Uterus often globally enlarged
Definition of lesion	Ill-defined in diffuse adenomyosis (adenomyoma may be well-defined)
Symmetry of uterine walls	Anterior-posterior myometrial asymmetry
Outline	Ill-defined
Shape	Ill-defined
Contour	Irregular or ill-defined
Rim	No rim
Shadowing	No edge shadows, fan shaped shadowing, linear hypoechoic striation
Echogenicity	Non-uniform Presence of intramyometrial: Mixed echogenicity Cyst Hyper-echogenic islands Subendometrial echogenic lines Buds
Vascularity	Translesional flow Diffuse minimal or few vessels
Endometrial rim	Irregular or ill-defined Distorted or imprinted
3D-TVS	
JZ thickness	Thickened JZ: Maximum JZ thickness (JZ_{max}) > 6–8 mm Ratio of JZ (JZ_{max}/total myometrial wall thickness) ≥50 % Difference (JZ_{max}) − (JZ_{min}) = JZ_{dif} ≥4 mm
JZ regularity	Irregular or ill-defined Distorted
JZ interruption	Interrupted Infiltration of the JZ by hyperechoic endometrial tissue

2D-TVS Features of Adenomyosis

Continuous improvements in the resolution of transvaginal ultrasound have enabled a more detailed assessment of uterine architecture. This has facilitated the detection of myometrial features of adenomyosis which could not have been seen with older ultrasound equipment.

According to several studies, the following 2D-TVS features were considered associated with adenomyosis [1, 5, 10–13] (Table 9.1):

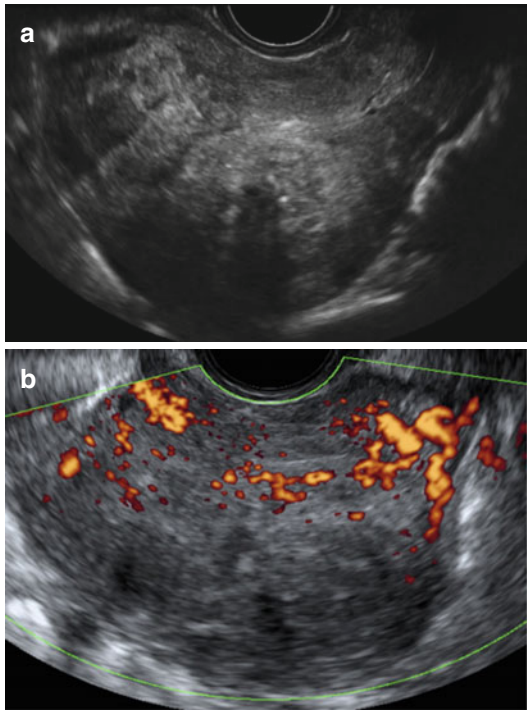

Fig. 9.1 Ultrasound images of a uterus with adenomyosis. (**a**) Gray scale image showing globally enlarged uterus unrelated to leiomyoma with irregular myometrial echotexture with hyperechoic irregular myometrial areas and small anechoic areas. Note the ill-defined endometrial stripe. (**b**) Power Doppler image showing diffusely spread vessels without the circular flow along a capsule that is typical for leiomyoma

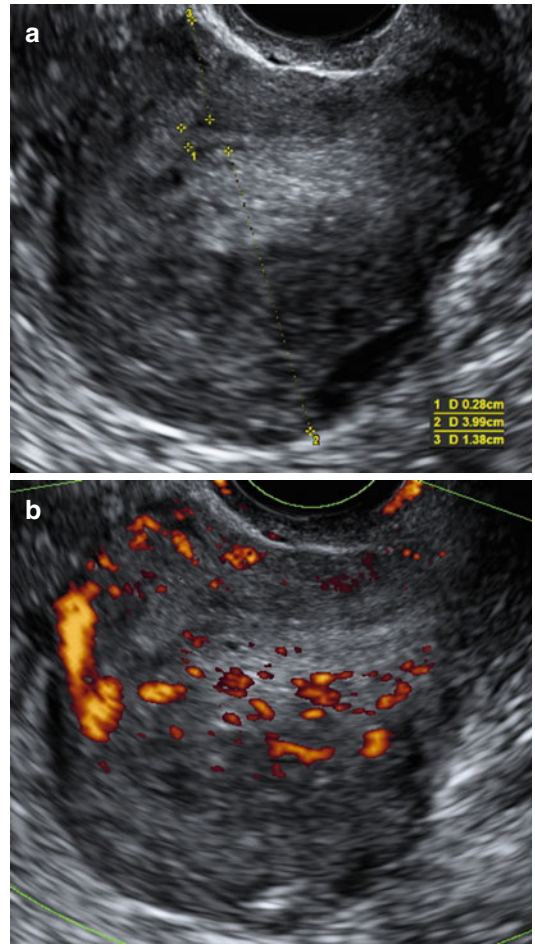

Fig. 9.2 Ultrasound images of a uterus with adenomyosis. (**a**) Gray scale image showing asymmetrically thickened, posterior wall (*2*) is thicker than anterior wall posterior uterine wall 3, with inhomogeneous, irregular myometrial echotexture due to hyperechoic and small cystic anechoic areas. Endometrial thickness (*1*). (**b**) Power Doppler image showing diffusely spread small vessels

- a globally enlarged uterus: the fundus of the uterus appears enlarged (Fig. 9.1)
- asymmetrically enlarged uterus (for example anterior wall thicker than posterior wall or vice versa) unrelated to leiomyoma (Figs. 9.1 and 9.2)
- round cystic area within the myometrium (Fig. 9.3)
- inhomogeneous, irregular myometrial echo texture in an indistinctly defined myometrial area with decreased or increased echogenicity; hyper-echogenic islands, subendometrial lines and buds (Fig. 9.4)
- myometrial hypoechoic linear striations seen as a radiating pattern of thin acoustic shadows not arising from echogenic foci or leiomyoma (fan shaped shadowing) (Fig. 9.3)
- indistinct, fuzzy endometrial-myometrial border (ill-defined endometrial stripe) (Figs. 9.1 and 9.2)
- presence of diffuse minimal vascularity seen as diffusely spread of small vessels which do not have the normal course of the arcuate and radial arteries inside the myometrium (Figs. 9.1, 9.2, 9.5, and 9.6)

Moreover, a new interesting sign called question mark form of uteri was reported recently [14]. This is described when the corpus uterus is flexed backwards, the fundus of uteri is facing the posterior pelvic compartment and the cervix is directed frontally towards the urinary bladder (Fig. 9.7).

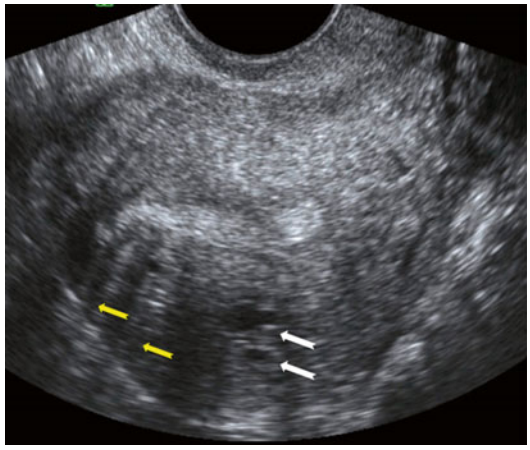

Fig. 9.3 Ultrasound image of a uterus with adenomyosis. Note the round cystic anechoic areas (*white arrows*) in the myometrium below the endometrium and hypoechoic linear striation (*yellow arrows*)

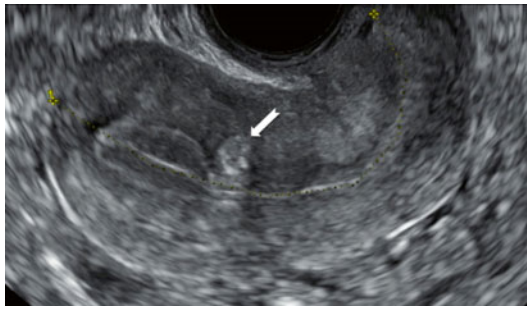

Fig. 9.4 Ultrasound image of a uterus with a hyperechoic buds (*white arrows*) in the myometrium beneath the endometrium

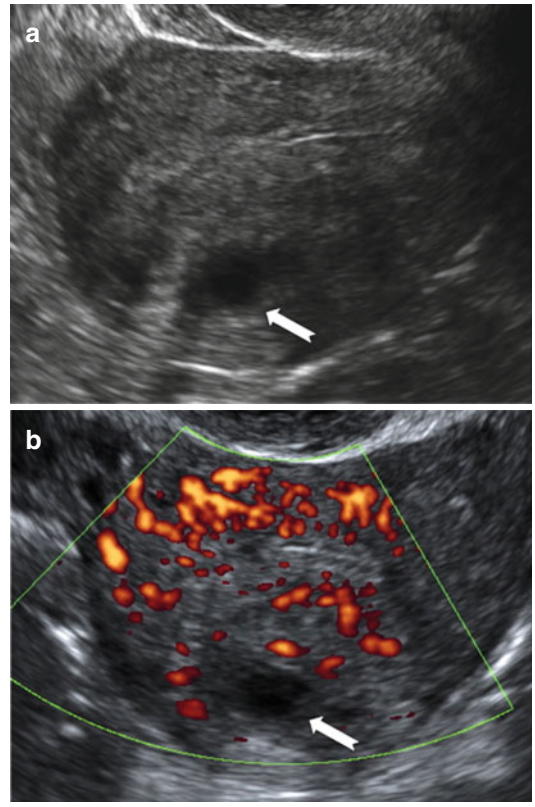

Fig. 9.5 Ultrasound images of a uterus with focal cystic adenomyosis of the posterior wall. (**a**) Gray scale image showing a cystic anechoic area in the myometrium of the posterior wall (*white arrow*). (**b**) Power Doppler image showing diffusely spread vessels around the cystic area (*white arrow*)

Power Doppler can be used to distinguish myometrial cysts from blood vessels and to discriminate between leiomyomas and focal adenomyosis (Figs. 9.5 and 9.6). Uterine leiomyomas feature circular flow along the myoma capsule, while localized adenomyosis and adenomyomas are characterized by diffusely spread vessels inside the lesions (Figs. 9.1, 9.2, and 9.8). Reinhold et al. reported that 2D-TVS had a sensitivity of 80–86 %, specificity of 50–96 %, and overall accuracy of 68–86 % for diagnosing diffuse adenomyosis [2]. However, 2D-TVS can yield equivocal result in the case of focal adenomyosis and in the presence of coexistent fibroids [1, 5]. A recent meta-analysis of 14 trials involving 1985 participants, reported the sensitivity and specificity of ultrasound diagnosed adenomyosis to be as high as 82.5 and 84.6 %, respectively [15].

Usually the diagnosis adenomyosis is made on histological examination of a uterus following a hysterectomy. The histological frequency of adenomyosis ranges from 5 to 70 % according to reported series. The wide variation is affected by the histological criteria and the number of sections examined. The majority of previous studies reporting the accuracy of 2D-TVS diagnosis of adenomyosis have assessed populations of women who underwent hysterectomy [1, 15, 16]. These included mainly women with severe symptoms who were more likely to have adenomyosis compared to the general population, and it is likely that the prevalence of adenomyosis in these studies is an overestimate.

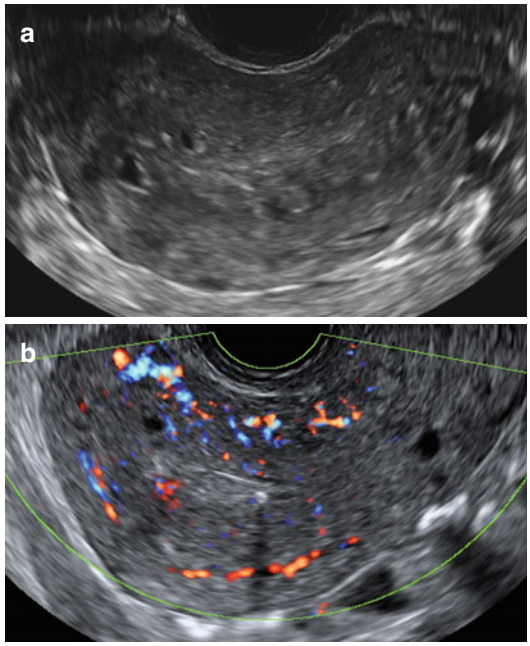

Fig. 9.6 Ultrasound images of a uterus with diffuse cystic adenomyosis of the uterus. (**a**) Gray scale image showing several small cystic anechoic areas and hyperechoic islands in the myometrium, note the ill-defined endometrial stripe. (**b**) Power Doppler image showing diffusely spread vessels in the affected myometrium

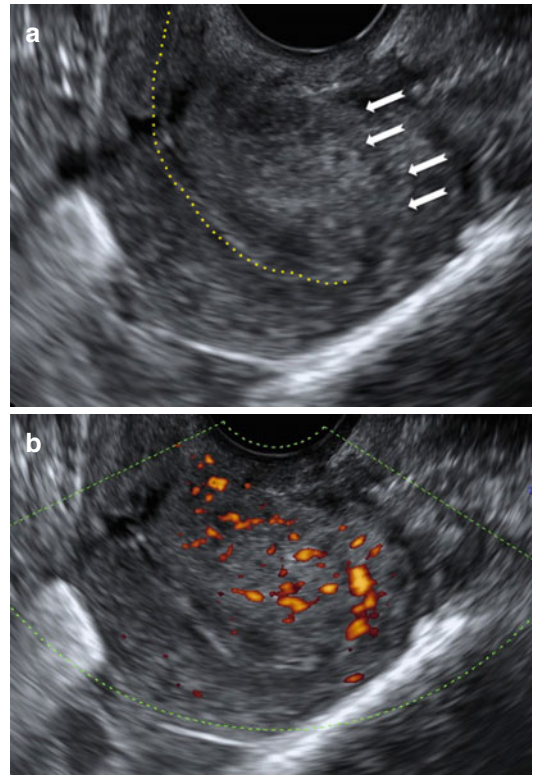

Fig. 9.7 Ultrasound images of a retroverted uterus with adenomyosis with the typical 'question sign'. (**a**) Gray scale image showing asymmetrically thickened posterior uterine wall with abnormal echogenicity (*white arrows*). (**b**) Power Doppler image showing diffusely spread small vessels

Furthermore, the 2D-TVS findings are more likely to appear in advanced stages of the disease. Most of the studies utilising TVS required the presence of at least two or three of ultrasound features for the diagnosis of adenomyosis [8, 9, 17–19]. But the presence of only one of the typical TVS features of adenomyosis raises some concern especially in young women (Fig. 9.9).

Targeted ultrasound guided biopsies have been proposed in an attempt to correlate histological findings to ultrasound features of adenomyosis in those younger women who will not undergo hysterectomy [20–22]. Recently, Nam and Lyu, performed abdominal ultrasound-guided transvaginal myometrial core needle biopsy in 1032 premenopausal women aged 22–53 years who had 2D-TVS findings suggestive for adenomyosis [22]. They reported a 92.26 % concordance rate between the transvaginal myometrial core needle biopsy and ultrasonographic diagnoses of adenomyosis [22].

The severity of adenomyosis is difficult to express in quantitative terms as the lesions are often poorly defined and may be disseminated throughout different parts of the myometrium. The number of different morphological features in an individual woman has been proposed as an indirect semi-quantitative measure of severity of adenomyosis [8, 19].

Tomassetti et al. defined a number of factors encouraging the development of adenomyosis including a history of spontaneous miscarriage, curettage, hysteroscopic resection of the endometrium, uterine myomectomy, caesarean section and the use of tamoxifen [23]. Furthermore, there are a number of studies that reported a correlation between ultrasound findings of adenomyosis and symptoms like menometrorrhagia or dysmenorrhea, infertility and multiparity has

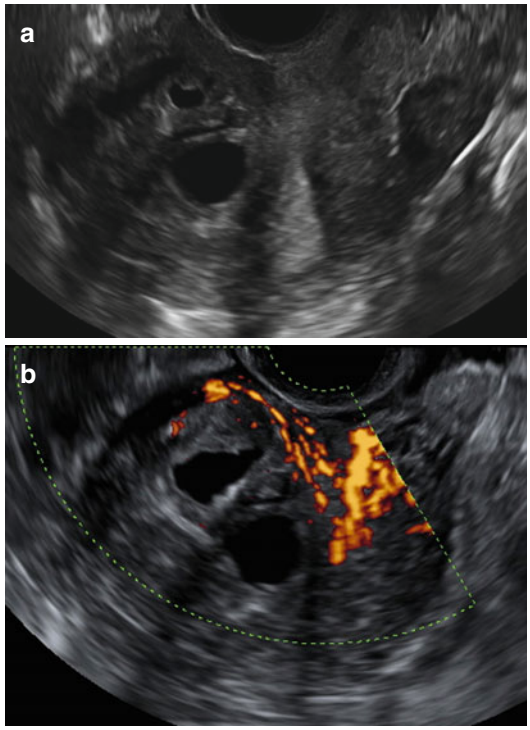

Fig. 9.8 Ultrasound images of a uterus with an anterior cystic adenomyoma. Gray scale image showing inhomogeneous, irregular myometrial echotexture with cystic areas (**a**). Power Doppler image showing more circular vessels in the hypertrophic myometrium surrounding the cystic areas (**b**)

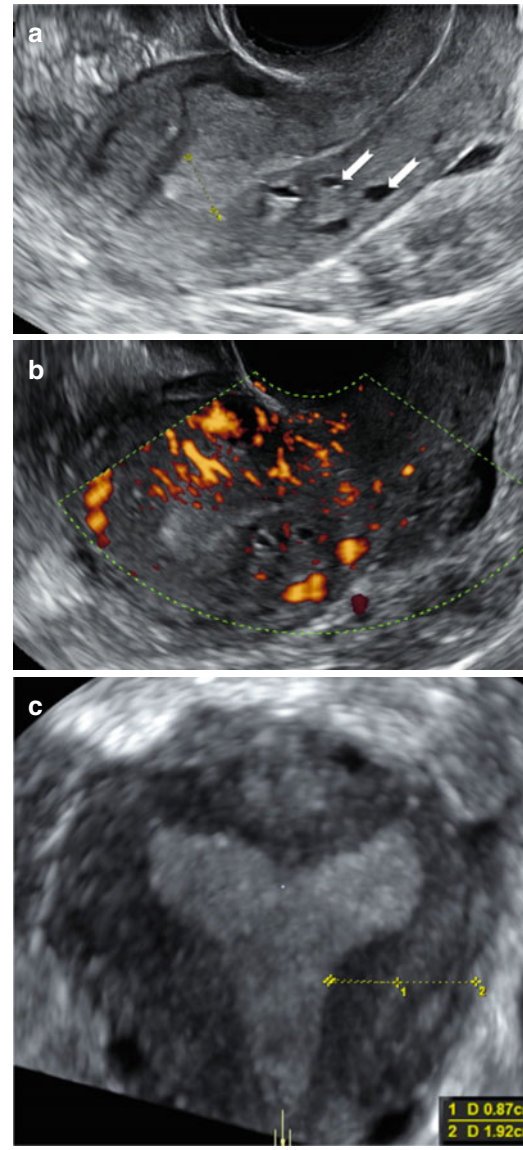

Fig. 9.9 Ultrasound images of a uterus in a 25 year old woman with cystic areas only in the posterior wall (*white arrows*). Gray scale image (**a**) and Power Doppler image (**b**) showing diffusely spread small vessels surrounding the cystic areas. Coronal section (**c**) obtained by 3D ultrasound of the same uterus showing a thickened JZ

been shown [24–26]. Therefore the association with symptoms could improve the diagnostic accuracy of ultrasound features for adenomyosis [8, 19, 24].

Adenomyosis seems also to be associated with endometriosis [17, 27, 28]. According to some authors, adenomyosis seems to share pathogenic mechanisms as well as similar symptoms (menometrorrhagia dysmenorrhea, dyspareunia, abnormal uterine bleeding and infertility), with endometriosis [27, 29, 30]. Knowing the prevalence of adenomyosis in a population with endometriosis helps in evaluating the likely contribution of adenomyosis to their symptoms.

Di Donato et al [2014] reported recently on a series of patients undergoing surgery for endometriosis a prevalence of adenomyosis diagnosed by ultrasound of 21.8 %. This prevalence is slightly higher than the prevalence (20.9 %) reported by Naftalin who evaluated patients attending a general gynecological ultrasound unit [28]. An interesting feature is the strong association between deep infiltrating endometriosis and adenomyosis reported in some recent studies [17, 31]. In a recent study, Lazzeri et al. confirmed the strong association between adenomyosis diagnosed by transvaginal

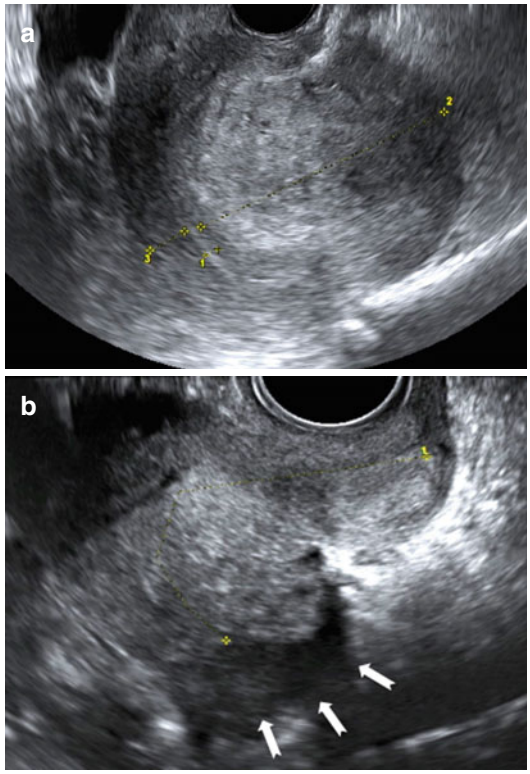

Fig. 9.10 Ultrasound images of a retroverted uterus with adenomyosis with the typical 'question sign'. (**a**) Grayscale image showing asymmetrically thickened posterior uterine wall (*2*) with abnormal echogenicity, (*1* endometrila thickness, *3* thicknes of the anterior uterine wall). (**b**) Posterior deep infiltrating lesions (*white arrows*) involving the adenomyotic myometrium and infiltrating the rectal wall posteriorly

ultrasound and endometriosis. The incidence of adenomyosis in patients affected by deep infiltrating endometriosis was 48.7 % [17]. Di Donato et al. found that the ultrasound 'question mark sign' of the retroverted fixed uterus, was strongly related to posterior deep infiltrating endometriosis (Fig. 9.10) [14].

Two dimensional transvaginal sonography has now achieved a high level of accuracy and many authors have reported high agreement between ultrasound diagnosis of adenomyosis and histological findings. A recent review concluded that transvaginal sonography should be the primary tool for the diagnosis of adenomyosis, with MRI being reserved for cases where TVS is inconclusive or in the presence of large fibroids [1].

3D-TVS Features of Adenomyosis

Although the junctional zone (JZ) can be visualized on 2D-TVS, acquisition of a 3D-TVS-volume enables more complete assessment in the sagittal, transverse and coronal planes as shown in a standardized multi-planar view [7, 9, 13] (Fig. 9.11). 3D-TVS signs of adenomyosis are based on the evaluation of the junctional zone on the acquired volume of the uterus in order to obtain the coronal view. In the coronal view, the junctional zone appears as a hypoechoic zone around the endometrium. Using the volume contrast imaging (VCI) modality with 2–4 mm slices the JZ can be seen clearer in all planes of the multiplanar view, this is also the case in the longitudinal and transverse uterine sections where the anterior and posterior junctional zones could be evaluated [8, 9, 13] (Fig. 9.11). The standardized multi-planar view which may be obtained by the z-rotation technique, is used in clinical practice for the evaluation of the coronal view as it reduces inter-observer variation in measurements. Imaging of the JZ may be optimized by using a post-processing rendering mode, for example VCI. The thickness of the slices or render box may be selected between 1 and 4 mm [8, 9, 13].

The JZ may be regular, irregular, interrupted, not visible, not assessable or may manifest more than one feature (e.g. irregular and interrupted). Any irregularity in the JZ can be described (e.g. cystic areas, hyperechogenic dots, hyperechogenic buds and lines) in each location of the uterus (anterior, posterior, lateral left, lateral right, fundus) [8, 9, 13] (Table 9.1).

In order to avoid reliance on subjective morphological descriptions of the JZ in terms of irregularity and infiltration, objective parameters were proposed. These include measurement of the thickness of the JZ in a manner familiar to the case of MRI evaluation [9, 32, 33]. The JZ and the total myometrial wall thickness can be measured perpendicular to the endometrium in the same section through the uterus. The maximum *thickness* of the junctional zone (JZ_{max}) is measured at the area where the JZ appears to be at its thickest, and the minimum thickness (JZ_{min})

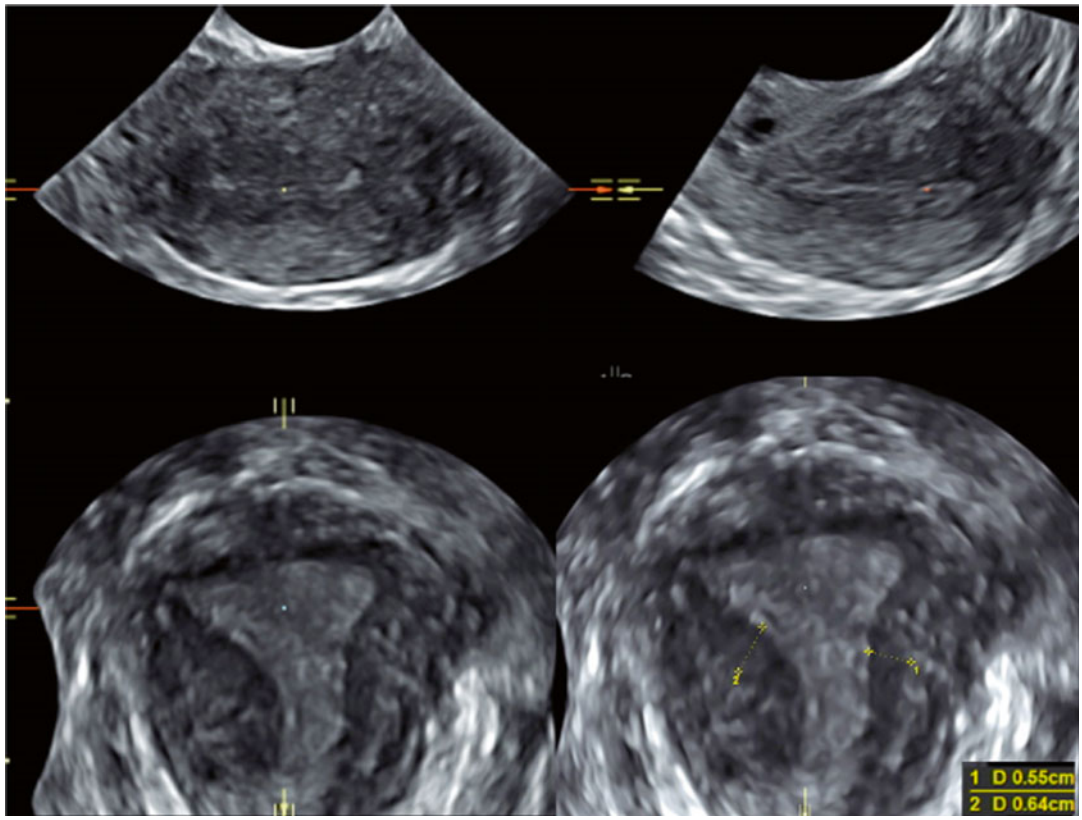

Fig. 9.11 Ultrasound image of the uterus obtained using three-dimensional ultrasound and volume contrast imaging (VCI) with 4 mm slices. A multiplanar view is shown: transverse and coronal sections of the uterus are shown on the *left side* of the image, a longitudinal section is shown on the *right side* of the image. The thickened junctional zone appears as a hypoechoic zone surrounding the endometrium. 2D ultrasound features of adenomyosis are not clearly seen in the longitudinal and transverse sections. However, in the coronal section, a slightly thickened distorted junctional zone is seen on the left

is measured where it appears to be at its thinnest after evaluation of the total three-dimensional volume of the uterus (Fig. 9.6). To define the *ratio* between the JZ and the total uterine wall thickness, both the JZ and the total uterine wall thickness should be measured using the same image [9, 13, 33]. The *magnitude* of JZ irregularity is expressed as the difference between the maximal and minimal JZ thickness: $(JZ_{max}) - (JZ_{min}) = JZ_{dif}$. The *extent* of JZ irregularity can reported as the subjective estimation of the percentage of the JZ that is irregular (<50 % or ≥50 %) [9, 13, 33] (Fig. 9.12). Detailed morphological measurement of the JZ is currently only relevant in the context of research protocols.

Interruption of the JZ may be caused by focal infiltration of the JZ by endometrial tissue, but contractions and changes within the JZ may also give rise to apparent JZ irregularities or influence measurement of JZ thickness. The extent of interruptions is recorded as a subjective estimation of the percentage of the JZ that is interrupted (<50 % or ≥50 %) [13] (Figs. 9.13 and 9.14).

Several studies have illustrated the sensitivity and specificity of 2D-TVS in diagnosing adenomyosis, but 2D-TVS generally describes alterations of the outer myometrium and does not consider alteration of the junctional zone. JZ, however, forms the basis for MRI diagnosis of adenomyosis. The study by Kepkep et al., (2007) was the only report that included poor

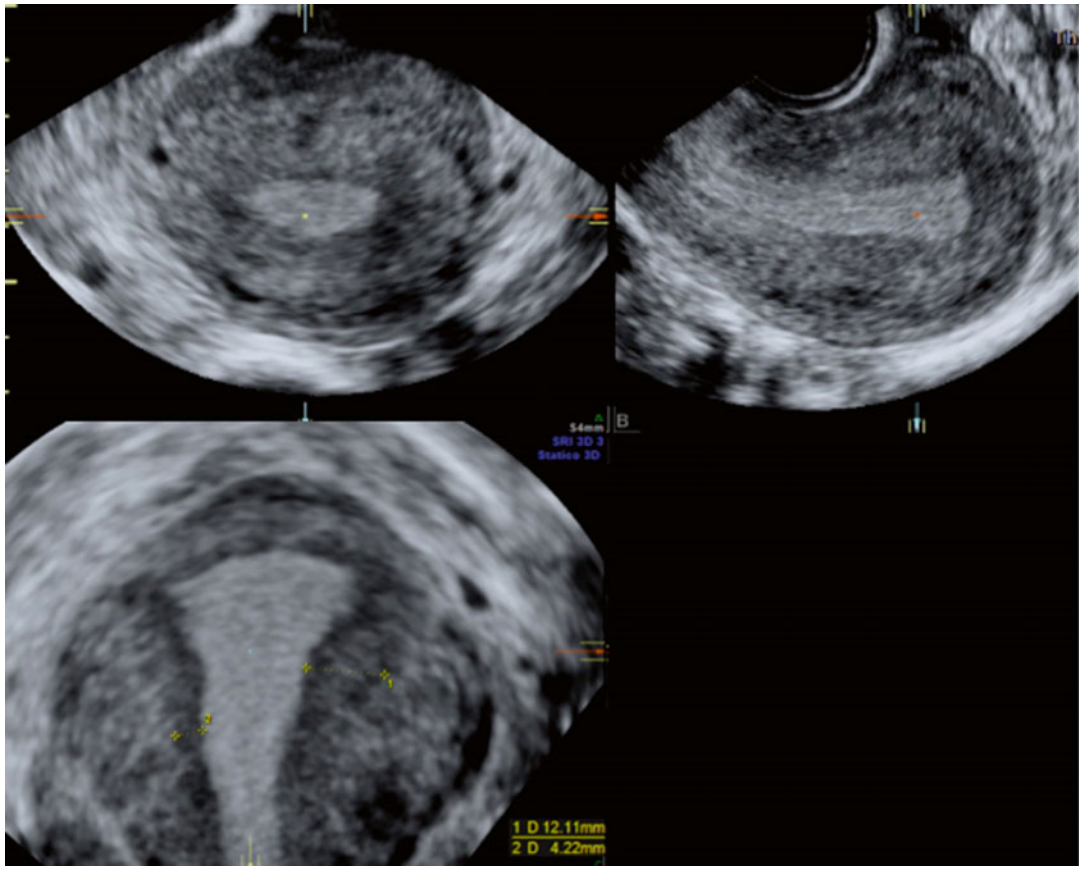

Fig. 9.12 Ultrasound image of the uterus obtained using three-dimensional ultrasound. A multiplanar view is shown: transverse and coronal sections of the uterus are shown on the left side of the image, a longitudinal section is shown on the right side of the image. 2D ultrasound features for adenomyosis are not clearly seen in the longitudinal and transverse section. However in the coronal section a thickened junctional zone is seen on the right side (1 = 12 mm = JZ_{max}) and a normal junctional zone is measured on the left side (2 = 4 mm = JZ_{min}). (JZ_{max}) − (JZ_{min}) = 8 = JZ_{dif}

definition of the JZ as a diagnostic feature in assessment of the accuracy of various 2D-TVS findings in adenomyosis [12]. They found that poorly definition of junctional zone had a high specificity (82 %) but a low sensitivity (46 %) in its diagnosis [12]. Three dimensional reconstruction of uterine anatomy in the coronal plane provides a new view of the junctional zone [7, 9]. Comparing transvaginal sonographic features to histology of the uterus after hysterectomies it was shown that junctional zone thickness $JZ_{max} \geq 6$–8 mm and (JZ_{max}) − (JZ_{min}) ≥4 mm were more significantly associated with adenomyosis compared to other 2D-TVS features [9, 33] (Fig. 9.12). Also, subjective evaluation of infiltration and disruption by endometrial tissue in the junctional zone is an accurate tool for the diagnosis of adenomyosis [7, 9, 33, 34] (Figs. 9.13, 9.14, and 9.15).

Thickening and disruption of the junctional zone are strongly associated with uterine adenomyosis [7, 9, 33] (Figs. 9.13, 9.14, and 9.15). Considering the hypothesis that adenomyosis is more likely to be caused by 'invasion' of endometrial tissue across the junctional zone and into the myometrium [29] 3D-TVS evaluation of junctional zone may be able to detect early adenomyosis [34] (Figs. 9.11 and 9.12). It has been reported that pelvic endometriosis, especially in advanced stages, is also strongly associated with junctional zone thickening and adenomyosis [9, 32, 34, 35]. Alterations of the junctional zone are

correlated with adenomyosis and may be involved in the process that determines pelvic endometriosis [27, 29, 35, 36].

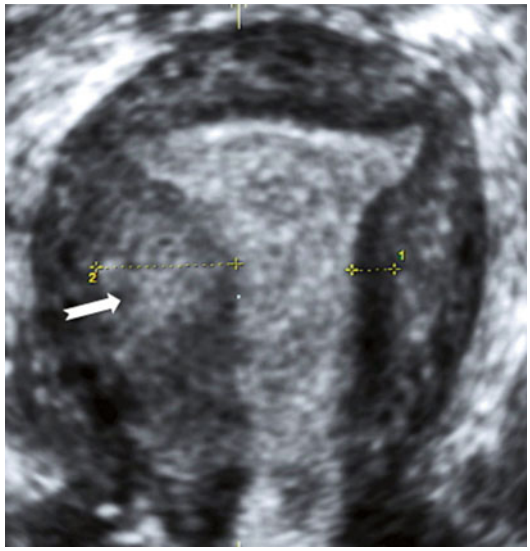

Fig. 9.13 Coronal view of a uterus obtained using three-dimensional ultrasound. A focal hyperechoic infiltration and thickening of junctional zone (*2*) is seen on the left side (*white arrow*) and a normal junctional zone is measured on the right side (*1*)

Therefore the evaluation of junctional zone and its alterations by non-invasive imaging seems very important especially in patients with suspect of pelvic endometriosis and adenomyosis. Three dimensional transvaginal sonography seems to be more accurate than conventional 2D-TVS for the diagnosis of adenomyosis and has the potential to evaluate early stages of the disease. As such, 3D-TVS should be considered in counselling and planning treatment of patients with deep endometriosis [34].

Using 3D ultrasound adenomyosis, junctional zone hyperplasia and adenomyotic cysts can now be detected in younger patients during their reproductive years (Figs. 9.11 and 9.12). The use of 3D transvaginal ultrasound for the diagnosis of junctional zone abnormality or adenomyotic pathology has been extensively described [9, 32, 34] and can now be used in patients seeking fertility treatment. As more women are postponing pregnancy into their third and fourth decades, an increasing proportion of women with fertility problems will have adenomyosis [26].

Recently, the possibility has been proposed of the use of hysteroscopy for the diagnosis and resection or ablation of intramural cystic

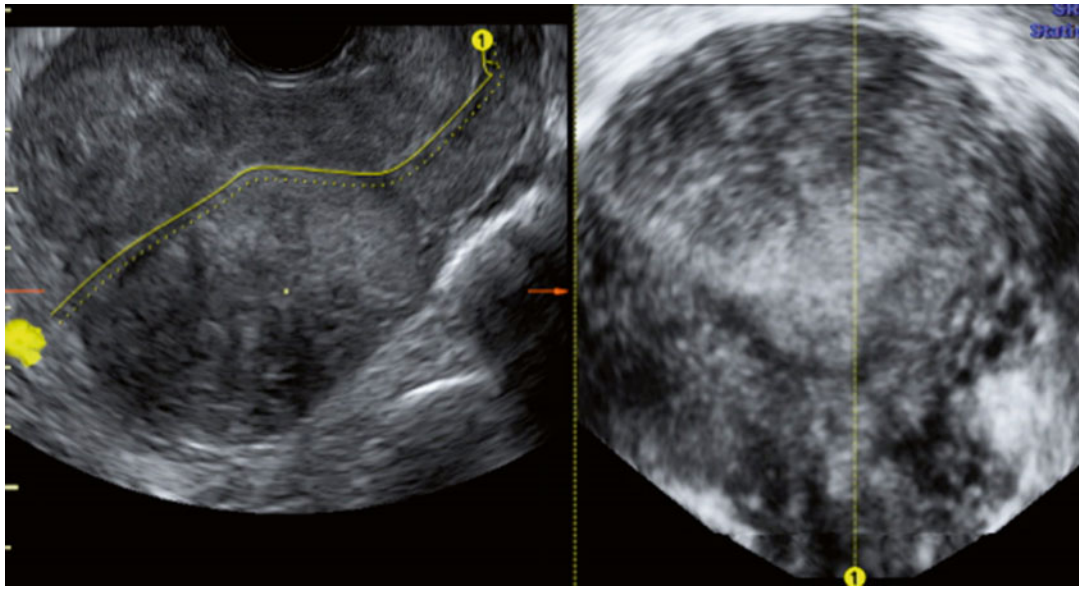

Fig. 9.14 Ultrasound image of the uterus with adenomyosis. On the *left*, a longitudinal section of a globular enlarged uterus with asymmetrically thickened of the uterine wall and with diffuse inhomogeneous, irregular myometrial echotexture and presence of hyperechoic areas. On the *right* the coronal section of the same uterus (*red arrow*) (obtained by a manual cut with Omni view modality of the 3D uterine volume), the junctional zone appears irregular, ill defined and completely infiltrated by the adenomyosis

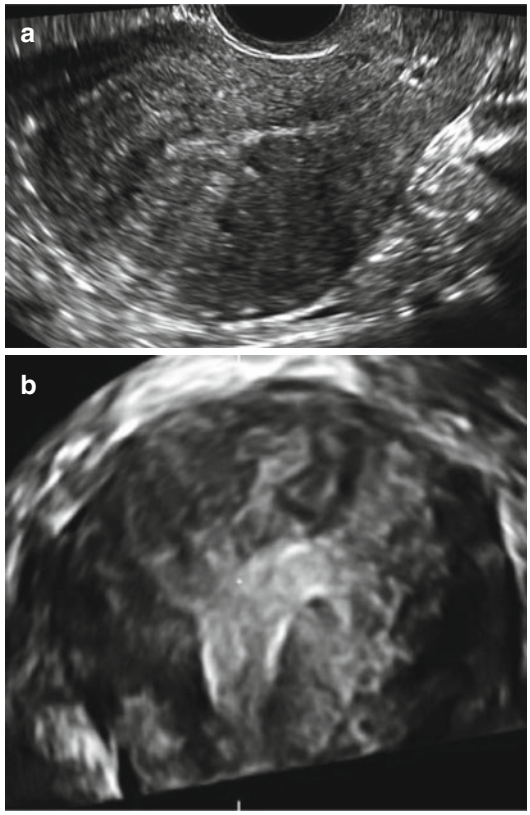

Fig. 9.15 Ultrasound image of the uterus with adenomyosis. (**a**) Gray scale longitudinal section showed an asymmetrically thickened of the uterine wall and with diffuse inhomogeneous, irregular myometrial echotexture, and presence of small hyperechoic and cystic areas. (**b**) Coronal section of the same uterus, the junctional zone is irregular, ill defined and completely infiltrated by adenomyosis

adenomyosis [21]. Treatment can be performed by mechanical dissection or bipolar ablative surgery but careful inspection of the endometrial cavity and evaluation of the uterine wall with special attention to the junctional zone using 2D-TVS and 3D-TVS is mandatory. The uterine spirotome proposed by Gordts allows a direct forward biopsy. Access can be gained to intramural cystic lesions that do not have visible intracavitary components under ultrasound guidance. Ultrasound guided hysteroscopy also offers an alternative for the treatment of subendometrial or junctional zone adenomyosis by localising cystic lesions, JZ hyperplasia or hyperechoic buds and thus minimizing tissue damage (Figs. 9.4, 9.9, 9.11, and 9.12).

Conclusions

Two dimensional transvaginal ultrasound has achieved a high level of accuracy. A high level of agreement has been demonstrated between ultrasound and histological diagnosis of adenomyosis. The presence of different morphological features in an individual woman could be an indirect measure of the severity of disease. The presence of more than one 2D-TVS feature permits a diagnosis of adenomyosis with high level of confidence without the need for histological confirmation. Thus identified however mostly patients with severe disease.

Three dimensional ultrasound evaluation of the junctional zone and its alterations has an important place especially in patients in whom pelvic endometriosis and adenomyosis are suspected. Three dimensional transvaginal sonography seems to be more accurate than conventional 2D-TVS.

The association between more than two 2D-TVS-3D-TVS features of adenomyosis and symptoms (menometrorrhagia dysmenorrhea, dyspareunia, abnormal uterine bleeding), multiparity and endometriosis has been demonstrated. However further studies are needed in young and asymptomatic women and more research is needed to evaluate the diagnostic value of less extensive or isolated features. Especially in cases with infertility or in the presence of endometriosis, isolated 2D-TVS or 3D-TVS features of adenomyosis could be useful in the detection of early disease, monitor its progression and in patient counselling.

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