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Imaging of adenomyosis of uterus: What radiologist needs to know?

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ABSTRACT

Background: Adenomyosis of uterus is difficult to diagnose clinically because of nonspecific symptoms and signs. Accurate diagnosis can be achieved with imaging. *Objective:* To study imaging findings of adenomyosis of uterus by EVUS and MRI with histopathological correlation and to evaluate accuracy of EVUS and MRI in diagnosis of adenomyosis. *Material & Methods:* Prospective study of 50 patients in age group of 30-59 years, presenting clinically with menorrhagia, dysmenorrhea, pelvic discomfort, low backache and uterine enlargement underwent EVUS and MRI. Imaging findings were correlated with histopathology reports from biopsy and operated cases. *Results:* Adenomyosis of uterus was confirmed in 41 patients, 38 patients were diagnosed correctly on magnetic resonance imaging. MRI showed 2 false positive and 3 false negative diagnosis. EVUS correctly diagnosed 33 patients. It showed 4 false positives and 8 false negatives. Sensitivity of MRI was 92.68% and specificity was 81.82%. EVUS showed sensitivity of 80.49% ($p<0.001$) and specificity of 69.23% ($p=0.41$). *Conclusion:* EVUS and MRI are extremely accurate methods of diagnosing uterine adenomyosis. MRI is more precise than EVUS.

Keywords: Uterine Adenomyosis, Endovaginal ultrasonography, Magnetic Resonance Imaging, Uterine Enlargement, Uterine junctional zone.

1. INTRODUCTION

Adenomyosis of uterus is an important gynecological pathology. On histopathological examination there are heterotopias of endometrial glands and adjacent stromal tissue into surrounding myometrium along with hyperplasia of smooth muscles. There are no specific symptoms or signs on clinical examination, making it difficult to diagnose adenomyosis of uterus clinically. Role of EVUS & MRI in diagnosing cases with clinically highly suspicious adenomyosis of uterus can be established as follows: Firstly, the accurate diagnosis can be done with diagnostic imaging, whereas, uterus preserving treatment can be done in mild and uncomplicated adenomyosis. However, total hysterectomy is the management of choice for severe adenomyosis. Secondly, diagnostic imaging is important to measure the degree of involvement of myometrium. Measurement of extent of myometrial invasion is crucial for planning the management, because endometrial

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ablation therapy is highly effective in superficially invasive adenomyosis than in extensive adenomyosis. Thirdly, diagnostic imaging is useful for follow up of disease progression in cases who are undergoing medical line of treatment (Reinhold et al., 1999). Adenomyosis of uterus can be sometimes complicated by presence of fibroids, making it difficult to diagnose accurately by ultrasonography alone.

The line of management and prognosis of pathology is separate. Most of the clinicians more often choose medical management for adenomyosis alone, whereas, surgical management for adenomyosis with leiomyoma, especially if the uterus is bulky (Hanafi, 2013). Diagnostic imaging findings revealed by EVUS and MRI are correlated very closely to those demonstrated on histopathological diagnosis. Previous studies on diagnosis of adenomyosis by EVUS have noted sensitivity, specificity and diagnostic accuracy of 80-86%, 50-96% and 68-86% respectively (Brosens et al., 1995; Fedele et al., 1992; Reinhold et al., 1995). Many studies also found Magnetic Resonance Imaging more accurate in diagnosing adenomyosis showing sensitivity of 86-100% and specificity of 84-100% with diagnostic accuracy of 85-90% (Reinhold et al., 1996).

Aim of our prospective study is to demonstrate imaging characteristics of adenomyosis of uterus and to differentiate findings of uterine adenomyosis by EVUS & MRI with histopathological correlation from biopsy and operated cases and to evaluate the sensitivity, specificity, predictivity and accuracy of imaging modalities.

2. MATERIAL & METHODS

Our prospective, observational diagnostic study was conducted from February 2020 to February 2021 on 50 female patients of central India after approval by Institutional Ethics Committee (No. NKPSIMS & RC&LMH/IEC/5/2020). Patients of 30-59 years age group, presenting with complaints of menorrhagia, dysmenorrhea, pelvic discomfort, backache & uterine enlargement on clinical examination were included. Patients, clinically suspected of uterine adenomyosis were examined by EVUS and MRI. Histopathological correlation was obtained from biopsy and operated cases. EVUS was performed on high end Ultrasonography machine with high frequency EVUS probe (5-8MHz) to obtain high resolution quality uterine images for better demonstration of adenomyosis. The real time EVUS Ultrasonographic findings of adenomyosis were studied, as the findings may not be properly seen on static images. The normal uterine parenchyma shows different zones with varying Echo pattern.

The endometrial heterotopia in uterine adenomyosis arises from stratum basal layer of endometrium, which is a thin layer and difficult to demonstrate separately at ultrasonography. In adenomyosis the different uterine parenchymal zones show altered Echo pattern & distorted appearance. On EVUS, adenomyosis shows heterogeneous hypoechoic areas in myometrium. The hypoechoic areas represent hyperplasia of smooth muscles of myometrium at histopathological analysis. The heterogeneous areas correspond to small echogenic foci of heterotrophic endometrial tissue with hypoechoic smooth muscle surrounding it. The presence of ecstatic glands or small foci of hemorrhages within the endometrial heterotopic component results in formation of small cysts in myometrium (frequently less than 5 mm in size) (Reinhold et al., 1999). Additional EVUS features of adenomyosis are abnormality of uterine contour, ill-defined demarcation of abnormal and normal myometrial tissue and an oval or elliptical type of myometrial abnormality.

At least two of the following five criteria on EVUS are essential to diagnose adenomyosis of uterus. a) No distinction of endometrium-myometrium junction. b) Anterior and posterior wall myometrial asymmetry. c) Striations at sub endometrial-myometrial junction. d) Presence of cysts and fibrosis in myometrium. e) Heterogeneity of myometrial parenchyma (Fedele et al., 1992; Reinhold et al., 1995; Reinhold et al., 1996; Bazot et al., 2001; Bazot et al., 2002). 16 channel 1.5 Tesla MRI machine with dedicated pelvic multicoil array was used for performing MRI. High resolution thin section MRI images obtained with pelvic multicoil array were sufficient to diagnose adenomyosis. On MRI, the zone wise anatomy of uterus was optimally demonstrated on T2-weighted sequences in sagittal plane. In females of child bearing age, different zones of uterus can be demonstrated on T2-weighted image. On MRI adenomyosis was seen as hypointense lesions on T2 weighted image with focal or generalized widening of junctional zone.

Hypointense lesions represented hyperplasia of smooth muscles along with endometrial heterotopia. 12 mm and more maximum junction zone thickness confirmed adenomyosis, whereas, 8 mm and below junction zone thickness, ruled out adenomyosis. If maximum thickness of junction zone was between 8and 12 mm, other features, like focal thickening of junctional zone, ill-defined peripheral margins or small hyperintense lesions on T1 and/or T2 sequences were required to confirm adenomyosis.

To differentiate adenomyosis from leiomyoma was frequently difficult. On EVUS, features that favored adenomyosis were, ill demarcated borders, minimum mass effect, an oval or ellipse shape, no significant vessels near the borders, absence of calcification, whorled appearance, linear striations and hyperechoic nodules. On MRI, hyperintense linear foci were typical for adenomyosis.

Patients diagnosed as adenomyosis on EVUS and MRI underwent surgery or biopsy. Histopathological evaluation was done. The histopathological diagnosis of post-surgery/ post biopsy tissue was noted. Statistical tests like specificity, sensitivity positive and negative predictivity values and total accuracy was determined for EVUS and MRI in correlation with final histopathological diagnosis. Statistically significant P value considered was $p<0.005$

3. RESULTS

Our study included 50 females with clinical impression of adenomyosis and age ranging from 30-59 years. No significant difference was observed in patient gravidity of uterus, parity, height, weight, mean age in diagnosis groups. Adenomyosis was proved in 41 women. MRI correctly diagnosed 38 out of 41 patients. 3 pseudo-negative and 2 pseudo-positive diagnosis were observed with MRI. Sensitivity of 92.68% in diagnosing adenomyosis was observed on MRI. MRI showed specificity of 81.82%, positive predictivity value of 95% and negative predictivity value of 75% with total accuracy of 90.38%. Patients positively diagnosed as adenomyosis on MRI were 5.10 times more possibility of having adenomyosis. On the other side, patients not diagnosed as adenomyosis on MRI had 0.09 times less likely possibility of having adenomyosis. On MRI, the patients having adenomyosis showed 14.5 mm mean thickness of junctional zone thickness, whereas, patients without adenomyosis showed 7.2 mm mean junctional zone thickness ($p<.001$). The optimal value of junctional zone thickness for confirmation of adenomyosis on MRI was 12mm or more (table 1).

With EVUS, 33 out of 41 patients were correctly diagnosed as adenomyosis. 8 pseudo-negative and 4 pseudo-positive diagnosis observed. The commonest cause of pseudo negative diagnosis with EVUS was misdiagnosis of adenomyosis as leiomyoma. Sensitivity of EVUS to diagnose adenomyosis was found to be 80.49 % ($p< .001$) and specificity was 69.23 % ($p=.41$). The positive and negative predictivity value respectively was 89.19% and 52.94 % with total accuracy of 77.78%. Patients positively diagnosed as adenomyosis with EVUS had 2.62 time more possibility to have adenomyosis, whereas, cases not diagnosed as adenomyosis with EVUS had 0.28 times less possibility to have adenomyosis (table 2). This shows that, EVUS was more sensitive and less specific, which may be likely due to interference in diagnosing adenomyosis in cases with other uterine pathologies.

MRI was found significantly better ($p<.002$) than EVUS to detect adenomyosis. 33 cases were found true positive at EVUS, out of which 24 cases (73%) showed inhomogeneous myometrial echo texture and low attenuation areas without small cystic lesions. 7 cases (21%) showed low attenuation areas with small cystic lesions and 2 cases (6%) showed inhomogeneous areas in the myometrium. The mean length, an antero-posterior and transverse dimension were more in uterus with adenomyosis, than without adenomyosis, but was not found significant statistically. In adenomyosis, the mean posterior wall myometrial thickness was significantly more than mean anterior myometrial thickness (25.2 mm compared to 21.2 mm, $p<0.02$). So, we can consider that, an ill-defined inhomogeneous area in myometrium can be basis for adenomyosis (figure 1, 2 and 3).

Table 1 EVUS statistics (n=50)

Statistic	Value	95% Cl
Sensitivity	80.49%	65.13% to 91.18%
Specificity	69.23%	38.57% to 90.91%
Positive predictive value	89.19%	78.26 to 94.98%
Negative predictive value	52.94%	35.39% to 69.79%
Positive Likelihood Ratio	2.62	1.14 to 5.99
Negative Likelihood Ratio	0.28	0.14 to 0.58
Total Accuracy	77.78%	64.40% to 87.96%

Table 2 Magnetic Resonance Imaging statistics (n=50).

Statistic	Value	95% Cl
Sensitivity	92.68%	80.08% to 98.46%
Specificity	81.82%	48.22% to 97.72%
Positive predictive value	95%	84.39% to 98.52%
Negative predictive value	75%	49.35% to 90.23%
Positive Likelihood Ratio	5.10	1.45 to 17.91
Negative Likelihood Ratio	0.09	0.03 to 0.28
Total Accuracy	90.38%	78.97% to 96.80%

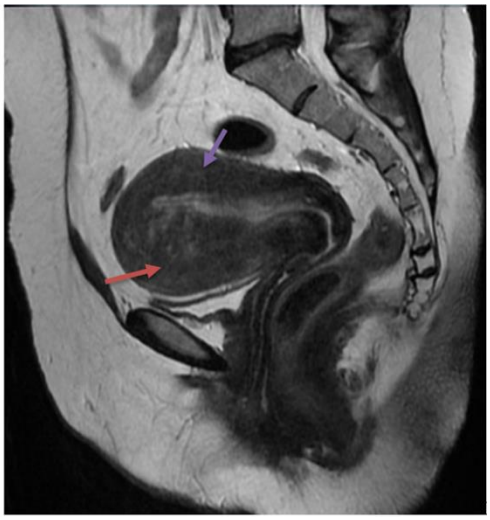

Figure 1 shows Uterine Adenomyosis on T2 weighted MR image in sagittal plane with increased thickness of anterior uterine wall (Red arrow) as compared to posterior uterine wall (purple arrow)

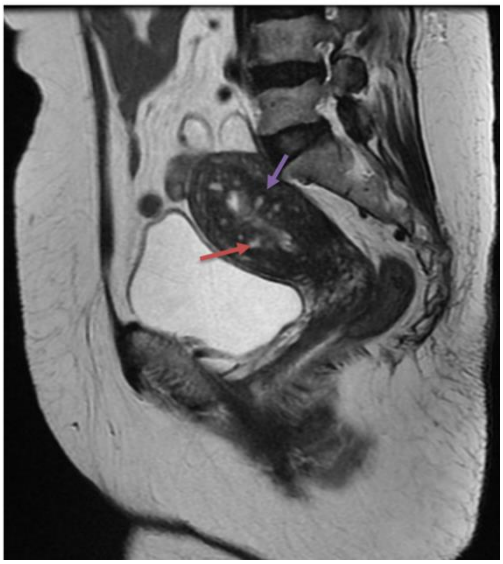

Figure 2 shows Uterine Adenomyosis on T2 weighted MR image in sagittal plane with increased number of cystic spaces (red arrow) and disruption of endo-myometrial junction (purple arrow)

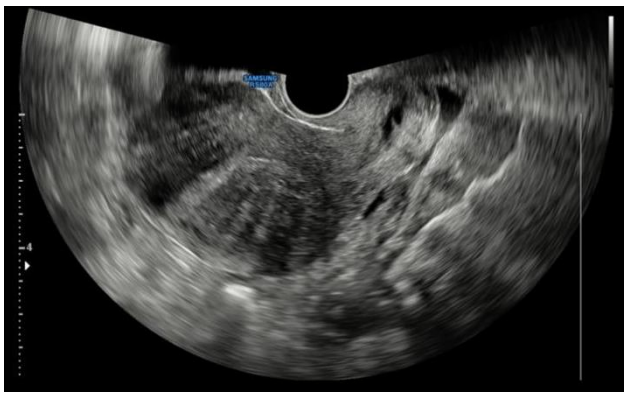

Figure 3 shows asymmetry of uterine wall with endometrial heterotropia in Uterine Adenomyosis on EVUS

4. DISCUSSION

In our study 50 females, in age group ranging from 30 to 59 years were studied with clinically suspected uterine adenomyosis. 41 patients were proved to be uterine adenomyosis. Accurate diagnosis was made on MRI in 38 cases out of 41 cases. 3 false negative and 2 false positive diagnosis were observed on MRI. On MRI, mean thickness of uterine junctional zone was 14.5 mm ($p<.001$) in patients having adenomyosis. In cases with no adenomyosis, the mean uterine junctional zone thickness was 7.2mm ($p<.001$). The optimum uterine junctional zone thickness for confirmation of adenomyosis with MRI was 12mm or more. The MRI sensitivity in detection of adenomyosis was 92.68% ($p<.001$), specificity 81.82% and 95% positive predictivity value with 75% negative predictivity value. Total accuracy of 90.38% was noted. With EVUS, adenomyosis was accurately diagnosed in 33 cases out of 41 cases. 8 pseudo-negative and 4 pseudo-positive diagnosis occurred. The sensitivity of EVUS for adenomyosis was 80.49 % and specificity of 69.23%. Positive predictivity noted was 89.19% and negative predictivity was 52.94 % with total accuracy of 77.78%.

The detectivity rate of adenomyosis reported by earlier studies had wide range which ranged from 8-85% (Hanafi, 2013; Brosens et al., 1995; Fedele et al., 1992; Reinhold et al., 1996; Ascher et al., 1994; Reinhold et al., 1995; Bazot et al., 2001; Atzori et al., 1996). The justification for these long ranges of values could be different histological evaluation parameters for demonstration of adenomyosis, the handling & processing of pathologic specimens and total sampling specimen blocks prepared. The various sample sizes, the modalities used for detection of adenomyosis, and variable exclusion and inclusion criteria used could also be attributed to long range of detectivity rate of adenomyosis.

Our study showed sensitivity of 80.49% and specificity of 69.23 % on EVUS for adenomyosis, but p value failed to reach the level of significance for specificity, proving that EVUS was sensitive but not specific enough as a diagnostic modality for diagnosing adenomyosis. In our study, the sensitivity correlated with previous studies, but the specificity was different from previous studies. This might be due to other uterine pathologies, especially uterine leiomyoma compromising the accuracy of EVUS for adenomyosis. Ascher et al., (1994) studied 20 females with clinical suspicion of adenomyosis.17 cases were having adenomyosis. Accurate diagnosis was done on MRI in 15 cases out of 17 cases. With EVUS, adenomyosis was correctly diagnosed in 9 cases out of 17 cases. 8 false negative diagnoses occurred. The most frequent cases of false negative diagnosis with EVUS were misinterpretation of adenomyosis with leiomyoma. They concluded that MRI is significantly better ($p<.002$) than EVUS in the diagnosing of adenomyosis.

Togashi et al., (1989) evaluated 93 females with clinically enlarged uterus on palpation and suspected for adenomyosis or leiomyoma. The MRI findings were consistent with operative and histopathological diagnosis. In 71 cases they found that, the uterus was enlarged due to leiomyoma whereas, in 16 cases the uterus was enlarged due to adenomyosis. Remaining 6 subjects had both lesions simultaneously. On T2 weighted MRI sequence, adenomyosis showed ill-defined inhomogeneous, predominantly hypointense, areas with hyperintense tiny spots within it. In 92 out of 93 females the cause of enlarged uterus was accurately demonstrated by MRI. They found that, MRI was almost completely accurate in differentiating leiomyoma from adenomyosis in cases having uterine enlargement. Reinhold et al., (1996) studied 119 patients who were undergoing hysterectomy. In 28 out of 119 cases, adenomyosis was confirmed as a reason of uterine enlargement. On EVUS the sensitivity was 89% and positive predictivity value 71% and negative predictivity value 96%, whereas for Magnetic Resonance Imaging the sensitivity was also 89%, positive predictivity value 65% and negative predictivity value 95%. The difference in sensitivity and specificity of EVUS and MRI was statistically not significant.

Togashi et al., (1989) also found that, making a diagnosis of adenomyosis preoperatively was a difficult task and in most of the cases histopathological examination was essential to confirm the diagnosis. Many authors also believed that it was difficult to differentiate adenomyosis from leiomyoma. However Magnetic Resonance Imaging was found highly accurate in demonstrating uterus abnormalities. In their study spin echo images with long transverse relaxation time demonstrated optimum details of zonal anatomy of uterus. They concluded that MRI was highly sensitive not only in the diagnosis adenomyosis but also in differentiating adenomyosis from leiomyoma. Magnetic Resonance Imaging played a crucial role in differentiating these lesions preoperatively and was also useful in offering appropriate management.

Reinhold et al., (1998) reviewed imaging appearances of adenomyosis. They also evaluated the limitations and role of presently available non-invasive imaging modalities and procedures including EVUS and MRI, in correctly diagnosing adenomyosis. They found that, the EVUS appearance of adenomyosis is actually due to hyperplasia of uterine smooth muscles associated with endometrial heterotopia and seen as hypoechoic areas on EVUS and hypointense areas on MRI. The endometrial heterotopia also helps in producing the imaging picture of adenomyosis. Due to availability of high-resolution machines, the frequency of detecting changes of adenomyosis has improved.

In the study of Atri et al., (2000) the adenomyosis prevalence was relatively more in premenopausal period. The study noted 81% sensitivity, 71% specificity, 90% positive predictivity, 54% negative predictivity and 74% accuracy on EVUS for detection of adenomyosis. However, the predictivity was dependent on prevalence. The hyperechoic areas represented specks of glands in endometrium and low echogenicity areas represented hyperplasia of myometrial muscles. They concluded that, myometrial asymmetry in thickness, echogenic nodules in subendometrial tissue and linear striations showed highest specificity and positive predictivity in case of adenomyosis.

Kepkep et al., (2007) observed in their study that, uteri with adenomyosis were frequently seen with leiomyoma and endometrial hyperplasia. The sensitivity reported was 80.8%, specificity was 61.4%, positive predictivity was 55.3% and negative predictivity was 84.4%. The specificity reported by them was lower as compared to studies by other authors. The different selection criteria for the diagnosing adenomyosis could be the factor responsible for different specificity and accuracy values on EVUS. In their study, linear striations in the subendometrial area showed highest specificity and positive predictive value and they considered this finding the most specific for diagnosis, although it's detection on Ultrasonography was uncommon. Their study subjects were restricted only to women considered for hysterectomy and there was no exclusion of cases with large and multiple leiomyomas which distorted the shape of uterus. These were the limitations of their study. Their study results suggested that, for uterine adenomyosis, inhomogeneous myometrial echotexture had higher sensitivity, whereas, a bulky uterus with globular shape, small cysts in the myometrium and linear subendometrial striations showed high specificity and positive predictive value.

Dueholm et al., (2002) reported that MRI was better than EVUS in the identification of uterine adenomyosis. MRI and EVUS were highly accurate in diagnosing adenomyosis. MRI accuracy was not dependent on uterine size and volume. MRI was better than EVUS in evaluating myometrial infiltration by sub endometrial cells. They considered histopathological diagnosis as gold standard in adenomyosis. Hirai et al., (1995) assessed various findings to differentiate malignancy from adenomyosis. They observed that, abnormal glands present in the endometrial basal layer were responsible for development of adenomyosis and cancers of endometrium sometimes may resemble adenomyosis, because both conditions are in continuity with endometrium. Adenomyosis showed either no contour or thin irregular contour. They introduced new scoring system which differentiated normal uterus, leiomyomas and adenomyosis. Their new system of scoring showed 91% sensitivity, 96% specificity and 94 overall accuracies in diagnosing adenomyosis.

5. CONCLUSION

Adenomyosis of uterus mainly occurs due to excessive growth of endometrial tissue which infiltrates in surrounding myometrium. EVUS and MRI are highly effective in adenomyosis. MRI is more accurate ($p<0.02$) compared to EVUS. On MRI, 12 mm or more thickness of uterine junctional zone strongly favors adenomyosis, whereas, 8 mm or less thickness of uterine junctional zone almost rules out adenomyosis. In uterine adenomyosis, EVUS is valuable, easily available, non-invasive modality. EVUS is more sensitive but less specific in adenomyosis. MRI is more indicated in indeterminate cases of EVUS and where uterus conserving treatment is considered.

Abbreviations

Endovaginal Ultrasonography (EVUS), Magnetic Resonance Imaging (MRI)

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Authors Contribution

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Ethical Approval

The study was approved by Medical Ethics Committee of NKP Salve Institute of Medical Sciences and Research Centre with the letter number: (NKPSIMS &RC & LMH/IEC/5).

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Conflicts of interest
The authors declare that there are no conflicts of interests.

Data and materials availability
All data associated with this study are present in the paper.

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