Distinct types of uterine adenomyosis based on laparoscopic and histopathologic criteria

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Summary

Purpose: To analyze laparoscopically treated cases of adenomyosis based on intraoperative and histopathology findings and to correlate different types with patients' presenting symptoms and characteristics, as well as with the surgical approach. *Materials and Methods*: Sixty-eight women who underwent laparoscopic treatment of adenomyosis at a referral center for gynecological laparoscopy. *Results:* Four distinct types of adenomyosis could be identified: diffuse, sclerotic, nodular, and cystic (54.5%, 13%, 28%, and 4.5% of cases, respectively). Menorrhagia as the main presenting symptom was significantly more frequent in patients with the diffuse type (84%) compared to those with sclerotic (44%) and nodular (37%) types ($p = 0.025$ and $p = 0.001$, respectively). All cases of cystic and nodular adenomyosis were treated by laparoscopic excision of the lesion. Eighty-nine percent of patients with sclerotic adenomyosis were treated with wide laparoscopic excision of the abnormal tissue. Eighty-one percent of patients with diffuse adenomyosis were treated with laparoscopic hysterectomy. Conclusions: Adenomyosis can be classified in four distinct types with differences in the presenting symptoms, as well as in the ideal surgical approach.

Key words: Adenomyosis; Laparoscopy; Laparoscopic adenomyomectomy; Laparoscopic hysterectomy.

Introduction

Uterine adenomyosis is a rather common gynecological disorder; the precise etiology as well as the mechanisms leading to the disorder are still not clearly determined. Clinical studies have proposed that adenomyosis results when endometrial glands invade the myometrial layer [1, 2]. In addition, Bird *et al.* suggested that the diagnosis of adenomyosis requires the identification of a smooth-muscle hyperplasia reaction [1]. It is postulated that disruptions of the endometrial-myometrial border allows for a reactive hyperplasia of the endometrial basalis layer and its extension into myometrium [3, 4]. Magnetic resonance imaging (MRI) can be useful for the detection of the junctional zone thickening, as well as for the evaluation of the myometrial invasion depth [5]. To date the main histopathologic criteria of adenomyosis are the existence of myometrial hypertrophy around a focus of adenomyosis and also the distance between the adenomyotic lesion and the endo-myometrial junction which has to measure at least the 25% of the total myometrial thickness [6].

Two distinct types of the disease have been described, diffuse and focal. The diffuse type is defined by the presence of multiple foci of adenomyosis distributed within the myometrium [3]. The focal type is defined by the presence of isolated nodules of hypertrophic myometrium and ectopic endometrium, also referred as adenomyomas. The current classification of adenomyosis has not been changed for almost a century when Cullen (1908) was the first who distinguished adenomyomas and diffuse adenomyomas [7]. Recent developments in diagnostic techniques [8], along with the wide application of endoscopic minimally invasive techniques in gynecology and the increased reports of uterus-sparing surgical procedures for the treatment of uterine pathology may alter the current management strategies for adenomyosis [9].

The aim of the present study was to analyze all the laparoscopically treated cases of adenomyosis in the present department based on intraoperative and histopathology findings and to correlate different types of the disease with patients' presenting symptoms and characteristics, as well as with the surgical approach.

Materials and Methods

The present study included all patients who had laparoscopic treatment for uterine adenomyosis at the Department of Gynecology, Lefkos Stavros Hospital, Athens, between January 2005 and June 2012. Sixty-eight patients were included in the study which was approved by the relevant institutional review board. All patients had a preoperative transvaginal sonographic (TVS) evaluation and were surgically treated by the same team of surgeons. All patients were treated either by laparoscopic excision of the lesion(s) or by subtotal laparoscopic hysterectomy, according to the preoperative and intraoperative clinical estimation of the extent and type of the adenomyosis and the patient's wish for future fertility. Diagnosis of adenomyosis was confirmed by histopathological examination in all specimens.

In patients treated with laparoscopic excision of adenomyosis with uterine preservation, the laparoscope was inserted into the abdominal cavity from an 11-mm supra-umbilical incision using the open access technique [10]. Three additional trocars were introduced under direct vision. After visual inspection of the pelvic cavity, the site of the uterine incision was determined by visual palpation of the uterus and based on the previous sonographic evaluation. Diluted vasopressin was injected (one ml of 20 U of vaso-

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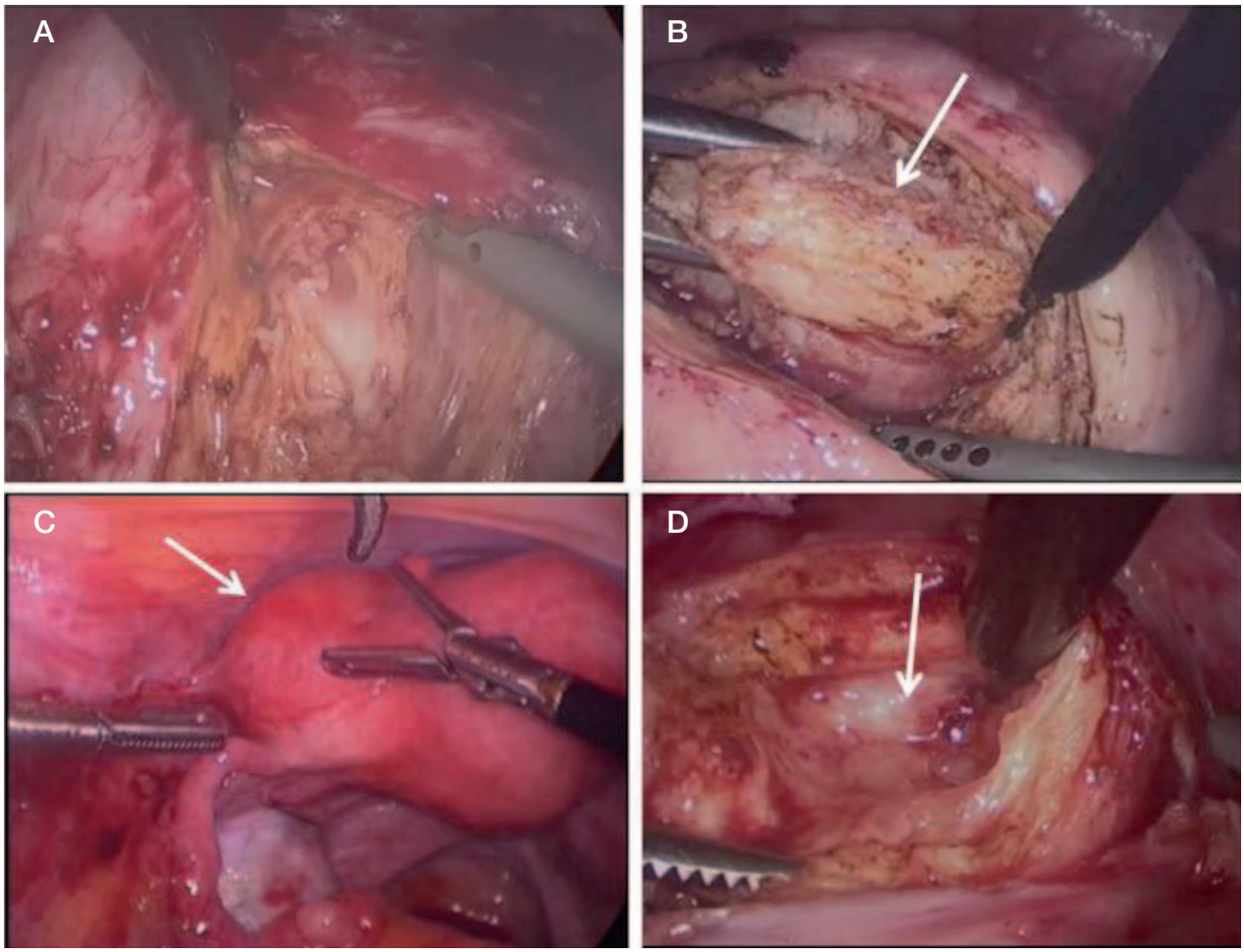

Figure 1. — Four types of adenomyosis identified during laparoscopy.
A: Diffuse. The entire myometrium has a spongiform texture.
B: Sclerotic. The lesion has an off-white fibrotic appearance (arrow).
C: Nodular. The arrow indicates a well-defined spherical lesion located on the left cornual region.
D: Cystic. The arrow indicates the base of the adenomyotic cyst.

pressin diluted with 40 ml of normal saline) in the myometrium around the affected area. The uterine wall was incised with monopolar current, set at 30 watts. The adenomyotic lesion was then isolated from the macroscopically healthy myometrium. Primary consideration was the removal of the whole adenomyosis while preserving as much unaffected myometrium as possible. Color and vascularity of the tissue was the main criterion used to identify the defective tissue. Adenomyotic tissue is paler, less vascular. and bleeds less due to fibrosis in contrast with unaffected tissue which is redder and more haemorrhagic. After resection was complete, the surgical wound was closed with deep interrupted 1-monocryl suture in one or two layers depending on the depth of the wound. The serosal layer was closed with either interrupted or continuous monocryl 0 or 2.0 sutures.

In patients treated with subtotal laparoscopic hysterectomy, the typical procedure was applied [11].

Haematoxylin and eosin stain was performed in the paraffin blocks that were obtained from the surgical specimens, in order to histologically identify the adenomyosis lesions. This was followed by Masson trichrome stain (Goldner with light green) to study the collagen and the smooth muscle fibers surrounding the adenomyosis foci (red: muscle fibers - green: collagen).

Statistical analysis was performed using the SigmaStat 2.03 software. Normality tests were performed and the data were analyzed using One Way ANOVA test, t-test, $\chi 2$ test, and the Fisher Exact Test, as appropriate. Yates Correction for continuity was performed where necessary.

Results

Depending on the macroscopic appearance and texture of the lesion(s) during laparoscopy, as well as on the respective histopathological findings, patients could be classified in four distinct types of the disease: diffuse, sclerotic, nodular, and cystic adenomyosis. In the ‘diffuse’ type (37 patients, 54.5% of study sample), the myometrium was uniformly affected and the size of the uterus was increased. During ex-

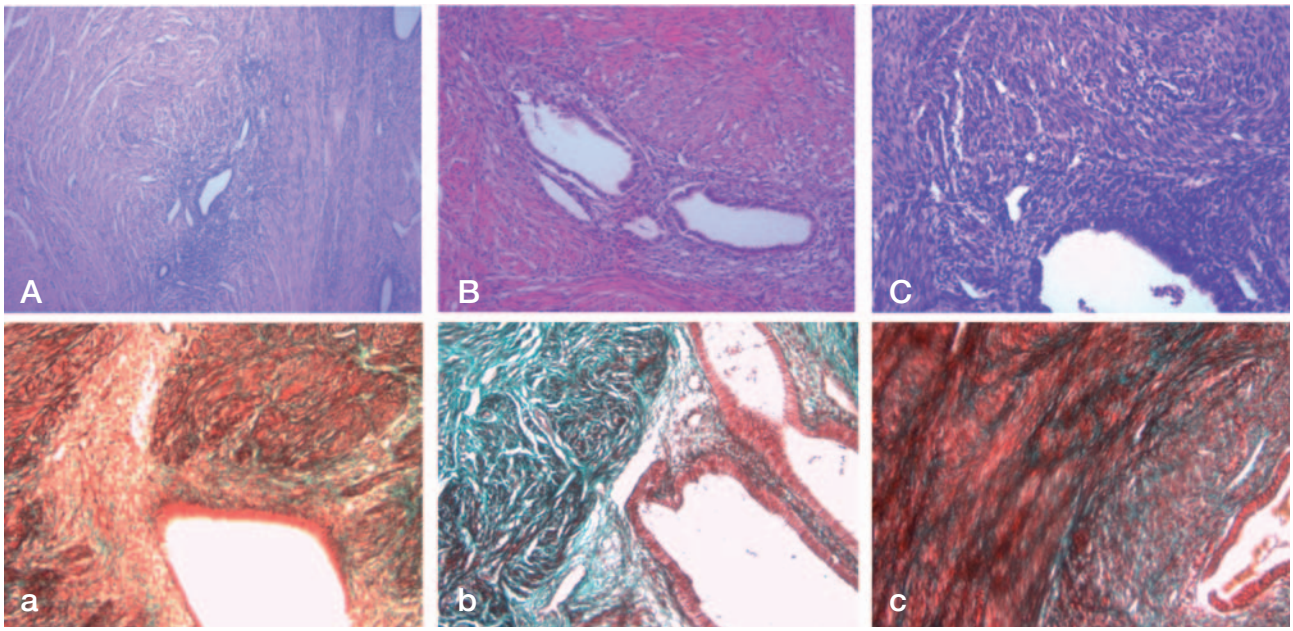

Figure 2. — Upper row represents haematoxylin and eosin stained specimens. A: Diffuse adenomyosis; an adenomyotic foci is demonstrated within normal myometrium. B: Sclerotic adenomyosis. C: Nodular adenomyosis; adenomyotic foci within leiomyomatous tissue.
Lower row represents specimens stained with the Masson trichrome histochemical stain. a: Diffuse adenomyosis; normal myometrium and smooth muscle fibers with bundled growth pattern are recognized surrounding the lesion. Scattered collagen fibers can be seen. b: Sclerotic adenomyosis; densely packed collagen fibers. C: nodular adenomyosis; densely arranged hyperplastic smooth muscle fibers; only a few collagen fibers are identified among the smooth muscle clusters.

Table 1. — *Patients' characteristics and main symptoms.*

Type	Age (yrs) Mean ± SD (Range)	Symptoms	
		Pelvic pain/ Dysmenorrhea n (%)	Menorrhagia
Diffuse	44.4 ± 6.0 (27-59)	7 (19)*	31 (84)*
Sclerotic	40.1 ± 6.4 (30-47)	5 (55)*	4 (44)*
Nodular	37.7 ± 5.2 (27-45)	13 (68)*	7 (37)*
Cystic	30.7 ± 2.5 (28-33)	2 (67)*	1 (33)*
Total	41.2 ± 6.7 (27-59)	27 (40)**	43 (63)**

*percentage of cases with the specific type of adenomyosis; **percentage of all cases of adenomyosis.

cision, the lesion had a spongiform texture (Figure 1A). Histopathology revealed multiple variable-sized foci of adenomyosis in the entire uterine wall with no hyperplasia of the smooth muscle cells. Adenomyotic lesions were spread in between normal myometrium. Smooth muscle fibers with bundled growth pattern were recognized surrounding the lesion (staining red - Figure 2A). Masson trichrome histochemical stain revealed only a few supporting collagen fibers (staining green- Figure 2a). In the 'sclerotic' type (nine patients, 13% of study sample) the lesion presented as an irregular thickening of the myometrium with an off-white pale fibrotic appearance (Figure 1B). It was firmly attached to the serosa and endometrium and, due to the hardness and friability of the tissue, grasping and suturing the tissue was difficult. Histopathology showed a segment of myometrium with multiple, variable sized foci of adenomyosis, surrounded by densely packed collagen fibers (probably as a degenerating phenomenon) with no hyperplasia of smooth muscle cells of the uterine wall (Figures 2B and 2b). In the 'nodular' type (19 patients, 28% of study sample), a spherical well defined lesion which was frequently located in the cornual region or the round ligaments was identified (Figure 1C). It represented a focus of adenomyosis with obvious hyperplasia of smooth muscle cells of the uterine wall, strangling the adenomyotic structure (probably due to reactive hyperplasia of the smooth muscle fibers (staining red, Figure 2C and 2c). Finally, in the 'cystic' type (three patients, 4.5% of study sample), the lesion had cyst characteristics, it was ≥ one cm in maximum diameter and it was independent of the uterine lumen (Figure 1D).

The characteristics and main symptoms of the study subjects are summarized in Table 1. The mean age of the patients was 41.2 years (SD: 6.7 years, min: 27 years, max: 59 years). Patients with diffuse adenomyosis (mean age: 44.4 years) were on average older than women with other types of the disease (sclerotic adenomyosis – mean age: 40.1 years, nodular adenomyosis – mean age: 37.7 years. Statistically significant difference in age was noted between patients with diffuse versus nodular adenomyosis ($p \leq 0.001$), as well as between patients with diffuse versus cystic adenomyosis ($p = 0.001$).

The main symptom in women with sclerotic and nodular type of adenomyosis was chronic pelvic pain and/or dys-

menorrhoea (55% and 68%, respectively) in comparison with only 19% of the women with the diffuse type; these differences were statistically significant ($p \leq 0.001$ and $p = 0.039$, respectively) (Table 1). On the contrary, the majority of patients (84%) with diffuse type of adenomyosis presented with menorrhagia refractory to conservative measures compared to 44% of patients with the sclerotic type ($p = 0.025$) and 37% of patients with the nodular type ($p = 0.001$).

Preoperative diagnosis of adenomyosis was established sonographically in 58 (85%) of the patients. The main indication for surgery was menorrhagia in 63% of patients, pelvic pain and/or dysmenorrhea in 40% of patients, and infertility in seven percent of patients. Diagnosis of endometriosis and fibroids had been made prior to surgery in nine and 34% of study subjects, respectively.

Laparoscopic removal of the defective adenomyotic tissue was the mode of treatment in 37 (54.5%) patients, while removal of the uterus was performed in 31 patients (45.4%). All (three) cases of cystic adenomyosis and all (19) cases of nodular adenomyosis were treated by laparoscopic removal of the adenomyotic lesion (adenomyomectomy) and reconstruction of the uterine body. Likewise, eight out of nine patients (89%) with sclerotic adenomyosis were treated with wide laparoscopic excision of the abnormal tissue and reconstruction of the uterine body. Only one patient (11%) with sclerotic disease and 30 out of 37 patients (81%) with diffuse adenomyosis underwent subtotal laparoscopic hysterectomy. No major complications occurred during or immediately after surgery.

Fibroids co-existed in 32.3% of the patients, more frequently in women with sclerotic (44%) and nodular (37%) adenomyosis than in those with diffuse adenomyosis (27%) and cystic (33%) adenomyosis, although the differences were not statistically significant. Concomitant endometriosis was present in 12% of patients with adenomyosis with no significant differences between the four types of the disease.

Discussion

Analyzing the laparoscopically treated cases of adenomyosis in the present study, on the basis of intraoperative and histopathology findings, four distinct types of the disease could be identified: diffuse, sclerotic, nodular, and cystic adenomyosis.

To date adenomyosis has been classified based on the distribution of the adenomyotic foci in the uterus [7]. When the lesions are spreading throughout the myometrium forming a large boggy uterus then adenomyosis is traditionally called ‘diffuse’. Adenomyomas are well-localized intramyometrial tumor-like lesions that resemble fibroids. This classification exists for almost a century with only addition the sporadic cases of cystic adenomyosis that are primarily affecting girls and young women [12, 13].

Dealing with several cases of traditionally called diffuse adenomyosis, the present authors have noticed distinct differences in the location, appearance, and texture of the adenomyotic tissue. There were cases where the entire myometrium was affected and the uterus had a balloon-like appearance. During dissection, the defective tissue was soft with a friable spongiform texture. The authors classified these women as having diffuse adenomyosis. In other cases, the disease was affecting only a segment of the myometrium with the rest of the uterus having a macroscopic healthy appearance. The defective tissue was hard with an off-white fibrotic appearance and was firmly attached to the serosa and endometrium. Although this type has also been described as focal or segmental adenomyosis [14], the authors referred to this type of adenomyosis as sclerotic adenomyosis. The diffused type affected the entire organ had no operative planes, therefore it was impossible to be resected. In contrast the sclerotic type, even though, its surgical margins were irregular, they could be identified due to the change of texture, color, and vascularity of the tissue. In retrospect these two groups of patients presented with different symptoms and, as expected, a wide resection of the disease with preservation of the uterus was feasible in cases of sclerotic adenomyosis. Based on the authors’ observations and according to the literature, they have included two additional types of adenomyosis, the so called “nodular adenomyosis” which refers to the traditionally called adenomyomas, and the “cystic adenomyosis” which represents the less frequent entity.

Differences in macroscopic appearance and tissue rigidity that were noticed during laparoscopy were subsequently confirmed by the histopathologic examination. In cases of diffuse adenomyosis the defective tissue was scattered along the entire myometrium. Only a few supporting collagen fibers were evident, which is a finding that partially explains the soft texture of the tissue. Nodular adenomyosis, on the other hand, presented as a rigid whitish tumor often resembling a fibroid. Densely packed hyperplastic smooth muscle fibers generated this leiomyomatous texture. The main histopathologic finding that distinguished sclerotic adenomyosis from the other two types of the disease was the high concentration of collagen fibers adjacent to the adenomyotic foci (Figure 3C). Based on the present clinical observation, there was an ascending degree of fibrosis from diffuse, to sclerotic, to nodular adenomyosis. This is partly explained by the smooth muscle hyperplasia which caused severe fibrosis in cases of nodular adenomyosis and the tightly arranged collagen fibers which resulted in a less prominent fibrotic appearance. Excess fibrosis may lead to the scarring, chronic pain and alteration of tissue function that are the characteristics of the disease [15].

Although a large proportion of patients with adenomyosis are asymptomatic [16], the disorder is known to be associated with menorrhagia and dysmenorrhea, which are both frequent indications for hysterectomy [17]. However these symptoms can be encountered in other associated pathologies, such as fibroids, endometriosis, and endometrial polyps and are considered non specific for diagnosis [18, 19]. In the present cohort, menorrhagia was the most common complaint, presenting in 63% of the cases, which is consistent with what has been reported in earlier studies

[3]. It has been hypothesized that the adenomyotic uterus is unable to contract properly during menses, resulting in increased blood loss [3]. According to that theory, diffuse adenomyosis which affects the entire uterine musculature is more likely to present with menorrhagia than focal adenomyosis. The present results indicated that menorrhagia was indeed the chief complaint in cases that were classified as diffuse. On the contrary in women with nodular, sclerotic, and cystic adenomyosis, pelvic pain and dysmenorrhea were the predominant symptoms. Therefore the authors suggest that adenomyotic lesions involving a part of the uterine body such as nodular, sclerotic. and cystic adenomyosis and also those that have a more dense and fibrotic consistency, such as nodular and sclerotic types, are more frequently associated with dysmenorrhea and pelvic pain compared to diffuse adenomyosis. The resemblance of nodular lesions with endometriotic rectovaginal nodules that has already been described enhances the relationship between this type of adenomyosis and pain [20]. This finding correlates with the already reported relation of pain with disruption of tissue architecture caused by fibrosis in cases of deep endometriosis [21].

The authors had a definite preoperative sonographic diagnosis in 85% of their patients which is in accordance with the positive predictive value (PPV) of TVS diagnosing adenomyosis reported in previous studies [22, 23]. TVS is usually the first choice of image modality when investigating cases of menorrhagia or pelvic pain, but accurate diagnosis of adenomyosis is not always possible, since correct recognition of the specific sonographic features of the disease is difficult [24, 25]. MRI is less observer dependent and thus considered a more accurate noninvasive technique for diagnosing adenomyosis [25]. Since gynecologists rely mainly on sonography to investigate a pathology, adenomyosis might be undiagnosed until after hysterectomy [26]. Moreover, up to 80% of adenomyotic uteri are associated with other benign proliferative conditions, such as endometriosis and fibroids [6], making preoperative diagnosis often problematic. Contribution of each disease to the symptomatology is difficult due to the similarity of symptoms in these conditions [16] and also due to the fact that adenomyosis is typically diagnosed only at the time of hysterectomy [19]. Concomitant adenomyosis in hysterectomy specimens of women with fibroids ranges from 15% to 57% [19, 27-29] and adenomyosis coexists with endometriosis in 28% of women or less [1, 30]. There were 22 (32.3%) women with fibroids and eight (12%) with endometriosis in the present study group. No correlation was made in the frequency of these conditions among different types of adenomyosis.

The choice of a less invasive surgical treatment in adenomyotic cases depends not only on the patient's wish for uterine preservation, but also on the surgical skills of the gynaecologist. Preoperative assessment of the topography and extent of the adenomyotic lesions is important. Because of limitations regarding visualization of the extent and location of adenomyosis, it is difficult to determine the feasibility and accuracy of complete excision when conserving the uterus. This is one of the main reasons why hysterectomy has been both the primary diagnostic and the therapeutic strategy for uterine adenomyosis [31]. Conservative surgery can be proposed in the majority of patients; however the current classification of adenomyosis is often limiting the surgical options to hysterectomy, especially in cases of diffuse adenomyosis. Advances in imaging technology and guided biopsy procedures [32], as well the increased demand of women in their forties for fertility preservation, allow and necessitate a less invasive form of treatment than hysterectomy. Uterine preservation was feasible in 54.5% of the presented patients. Diffuse adenomyosis accounted for the majority of patients that underwent a hysterectomy (30 out of 31 women). Laparoscopic resection of adenomyosis requires high expertise due to difficulty in recognizing the healthy margins of the tissue. It is essential to obtain an accurate preoperative diagnosis in order to refer the patient in a specialized center if necessary. Preoperative imaging and also change in appearance, vascularity or consistency of the tissue can guide the resection. Accurate preoperative diagnosis is essential.

Partial excision of adenomyosis during laparoscopy or laparotomy is an accepted mode of treatment in cases of cystic adenomyosis and adenomyomas [13, 33-35]. New operative techniques have been described and evaluated in relation to their feasibility and applicability [33, 36, 37]. In cases of diffuse adenomyosis however, hysterectomy is generally considered the only option. the authors consider sclerotic adenomyosis as an intermediate type of adenomyosis between diffuse and nodular which can be treated conservatively. They were able to do so in eight out of nine patients with sclerotic adenomyosis.

The main limitation of this study was the relatively small number of included patients; however, the present study may serve as a motivation for further research allowing for an updated and more detailed adenomyosis classification.

Conclusion

Contrary to the traditional two-type classification, adenomyosis can be actually classified in four distinct types (diffuse, sclerotic, nodular, and cystic) with significant differences in the presenting symptoms, as well as in the ideal surgical approach. Menorrhagia as the main presenting symptom is significantly more frequent in patients with the diffuse type compared to those with sclerotic and nodular types. All patients with cystic and nodular adenomyosis, as well as the majority of patients with the sclerotic type can be treated by laparoscopic excision of the lesion. The majority of patients with diffuse adenomyosis require treatment with laparoscopic hysterectomy.

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