Original

Review of Histological Variants of Uterine Leiomyomas seen in a Teaching Hospital

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Abstract

Background: Uterine leiomyoma is the commonest benign smooth muscle tumour of unknown aetiology and occurs mostly in reproductive-age women. The gross appearances are often altered by various degenerative changes and histological types of leiomyomas are of mainly interest as they may mimic malignancy in rare cases. This study described histopathological variants and degenerative changes of uterine leiomyomas seen at LTH, Ogbomoso over a 5- year.
Method: This was a hospital based retrospective study of 192 cases of uterine leiomyoma diagnosed histologically at the Department of Morbid Anatomy LTH, Ogbomoso between January 2012 and December 2016. Cases were retrieved from the histopathology register and demographic characteristics such as age were extracted. Leiomyomas were classified using 2014 edition of World Health Organization Classification of Uterine Smooth Muscle Tumour. Data obtained was analysed using both Microsoft Excel and Statistical Package for Social Sciences 23.0 (SPSS version 23.0).
Result: Leiomyoma was commonly seen the fourth decade of life which accounted for about 40.6%. Multiple nodules were found in 136(70.8%) cases. Intramural leiomyoma was the most common site accounting for 176(91.7%) cases. Usual leiomyoma was the commonest histological type accounting for 182(94.8%) cases. Degenerative changes were seen in 124 (64.6%) cases and hyaline change was the commonest secondary change with a frequency of 115 (59.9%).
Conclusion: Majority of women with uterine leiomyomas presented with multiple nodules. Intramural site was the most common location. Hyaline change was the most common degeneration and usual variant was the most common subtype seen in our study.

Keywords: Leiomyoma, degenerations, histological, variants, fibroids.

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Introduction

Uterine leiomyomas are benign tumours composed of smooth muscle cells. They occur mostly in women of reproductive age group.[1] The majority of patients with uterine leiomyomas have multiple leiomyomas, and each leiomyoma is believed to be clonal, arising independently from a single initiated smooth muscle cell.[2] Leiomyomas can be sub-serosal, sub-mucosal or intra-mural.[2]

Diagnosis of leiomyoma is usually clinical, though, ultrasonography is a cost -effective method that allows rapid diagnosis.[3] In routine clinical practice, myomectomy and hysterectomy specimens are sent to pathology laboratories where diagnosis of leiomyoma is confirmed. According to World Health Organization (WHO), leiomyomas can be classified histologically into following subtypes usual or conventional, cellular leiomyoma, leiomyoma with bizarre nuclei, mitotically active, hydropic, apoplectic lipoleiomyoma, leiomyoma, leiomyoma, dissecting (cotyledonoid), diffuse leiomyomatosis intravenous leiomyomatosis and metastasizing leiomyoma.[2,4]

Most published articles have explored the pathological features of leiomyoma worldwide and the review of literature has shown that less work has been done in Nigeria in comparison to other parts of the world.[5-10] The aim of the study was to describe histopathological variants and degenerative changes of uterine leiomyomas under review.

Method

Study Setting, design and population

The study was an hospital-based retrospective study of all cases of uterine leiomyoma diagnosed histologically at the Department of Morbid Anatomy, LTH, Ogbomoso, Oyo State. This is a tertiary health institution in the South-west geopolitical zone of Nigeria and the institution receives surgical specimens from Oyo, parts of Kwara and Osun states. All women with uterine leiomyomas diagnosed histologically were reviewed. Records of all cases of uterine leiomyoma within the study period were retrieved from the histopathology register, laboratory reports as well as case folders of patients where necessary. All cases of uterine leiomyomas with complete records were included in the study. Also, cases with incomplete biodata, missing blocks and slides were excluded. Diagnosis was confirmed by reviewing all slides by at least two histopathologists. The haematoxylin and eosin (H&E) stained slides of the corresponding cases and the paraffin-wax embedded tissue blocks were retrieved. Fresh H&E-stained sections were prepared in cases of faded, broken or missing slides. The H&E-stained slides were reviewed by the authors to confirm diagnosis and determine the histological and degenerative types according to 2014 World Health Organization histological classification of uterine leiomyomas. The variables such as age of patients, number and location of leiomyoma nodules, histological variants, and degenerative changes were collected using Microsoft Excel 2019.

Statistical analysis

Data obtained was analysed using both Microsoft Excel and Statistical Package for Social Sciences 23.0 (SPSS version 23.0). Data obtained from this study was presented in tables and chart. Frequencies of variables were calculated. Chi-square test was used to determine association between age group of patients and variables like number and location of nodules, histological variants and degenerative changes. P-value of less than or equal 0.05 was considered statistically significant.

Ethical Approval

Permission for the conduct of this study was obtained from the Ethical Review Committee of the LTH, Ogbomoso. This study was also performed in compliance with the guidelines of the Helsinki Declaration on biomedical research on human subjects.

Results

Leiomyoma was commonly seen among women of childbearing age, most commonly in the fourth decade of life which accounted for about 40.6%. In fifth decade, it accounted for 34.4%. (Table 1)

Single nodule was observed in 56(29.2%) cases while multiple nodules were found in the remaining 136(70.8%) cases. There was no significant association between the age of the patients and number of nodules with a p-value of 0.08. (Table 2)

Intramural leiomyoma was the most common site accounting for 176(91.7%) cases followed by submucosal in 25(13.0%) and subserosa in 23(12.0%) cases. Out of 192 patients studied, 26(13.5%) had nodules in more than one location with intramural and submucosal nodules accounted for 12(6.3%) while submucosal and serosal nodules accounted for 7(3.6%). There was a significant association between the age of the patients and submucosal location with a p-value of 0.008. (Table 2)

Usual leiomyoma was the commonest histological type accounting for 182(94.8%) cases while epithelioid leiomyoma was the least with 1 (0.5%) case reported. The usual variant was commonly seen in the fourth decade accounting for 76 (39.6%) of all leiomyomas studied. There was no significant association between the age of the patients and histological variants with a p-

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value of 0.194. (Table 3). Degenerative changes were seen in 124 (64.6%) cases. (Figure 1) The hyaline change was the commonest secondary change with a frequency of 115 (59.9%) while red degeneration was the least with a frequency of 3(1.6%). There was a significant association between the age of the patients and red degenerative change with a p-value of 0.000 (Table 2).

Table 1: Age distribution of patients with leiomyomas

Age group	*Frequency*	*Percentage*
20 to 29	17	8.90
30 to 39	78	40.60
40 to 49	66	34.40
50 to 59	22	11.50
60 and above	9	4.70
Total	192	100

Table 2: Age distribution and relationship between number of nodules, location of nodules, histological variants and degenerative changes seen in the study samples

Features	**Age Group (in years)**					**Total**	**X^2**	**P-value**
	20 to 29	**30 to 39**	**40 to 49**	**50 to 59**	**≥60**			
Number of nodules							8.35	.08
Solitary	3(1.6)	25(13.0)	17(8.9)	5(2.6)	6(3.1)	56(29.2)		
Multiple	14(7.3)	53(27.6)	49(25.5)	17(8.9)	3(1.6)	136(70.8)		
Location of nodules*							41.70	.23
Mucosal	0(0.0)	5(2.6)	16(8.3)	2(1.0)	2(1.0)	25(13.0)		
Mural	16(8.3)	70(36.5)	60(31.3)	22(11.5)	8(4.2)	176(91.7)		
Serosal	2(1.0)	7(3.6)	10(5.2)	1(0.5)	3(1.6)	23(12.0)		
Histological variants							25.19	.19
Cellular	0(0.00)	0(0.00)	1(0.50)	0(0.00)	1(0.50)	2(1.00)		
Epitheliod	0(0.00)	0(0.00)	0(0.00)	1(0.50)	0(0.00)	1(0.50)		
Hydropic	0(0.00)	1(0.50)	1(0.50)	0(0.00)	0(0.00)	2(1.00)		
Lipo-leiomyoma	0(0.00)	0(0.00)	3(1.60)	0(0.00)	0(0.00)	3(1.60)		
Myxoid	0(0.00)	1(0.50)	1(0.50)	0(0.00)	0(0.00)	2(1.00)		
Usual	17(8.90)	76(39.60)	60(31.30)	21(10.90)	8(4.20)	182(94.8)		
Degenerative changes*							2.96	.56
Hyaline	11(5.70)	47(24.50)	39(20.30)	13(6.80)	5(2.60)	115(59.90)		
Cystic	2(1.00)	9(4.70)	8(4.20)	1(0.50)	0(0.00)	20(10.40)		
Red	3(1.60)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	3(1.60)		
Calcification	1(0.50)	3(1.60)	5(2.60)	0(0.00)	2(1.00)	11(5.70)		
Inflammation	0(0.00)	4(2.10)	1(0.50)	1(0.50)	0(0.00)	6(3.10)		

*Multiple responses, # P-value of less than 0.05 is considered statistically significant.

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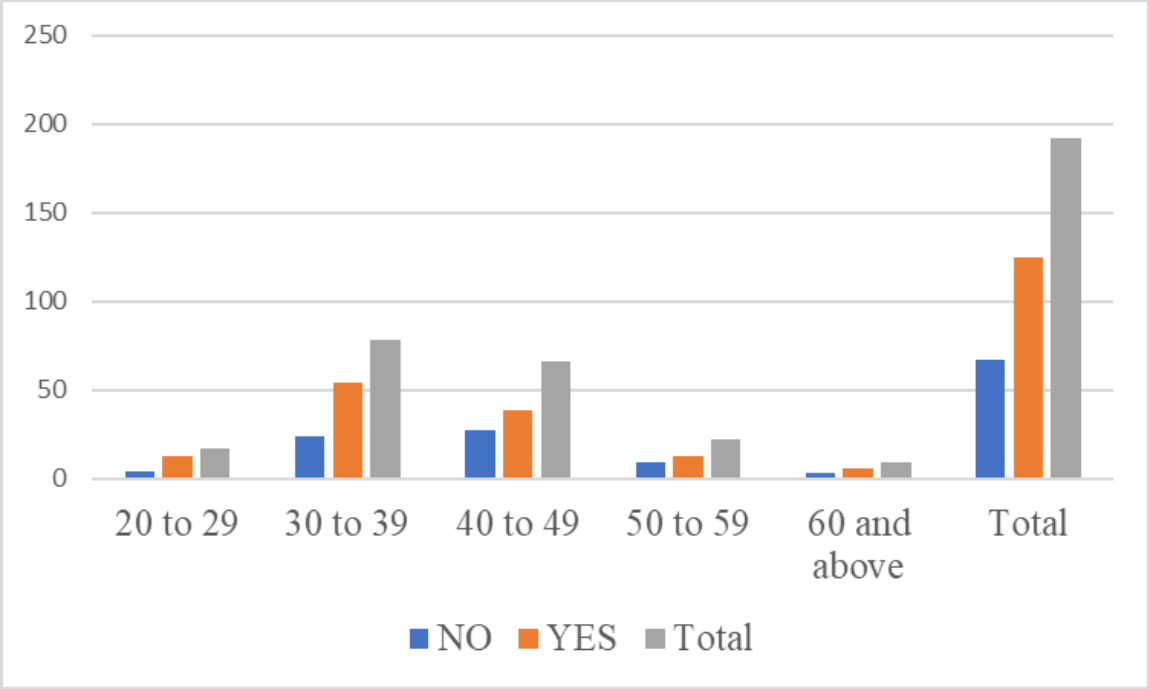

Figure 1: Bar chart showing a frequency of leiomyoma with degenerative changes. Yes and No, indicate the presence or absence of degenerate changes respectively.

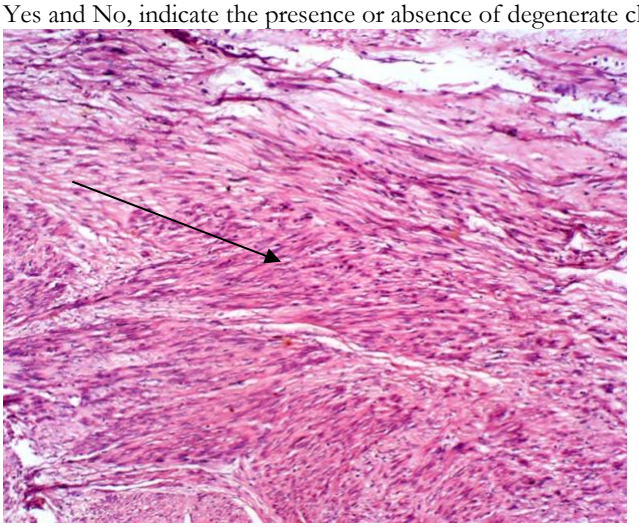

Figure 2: Photomicrograph showing histoarchitecture of the usual variant of uterine leiomyoma. Note the interlacing fascicles of smooth muscle cells with elongated nuclei and eosinophilic cytoplasm. H and E x400.

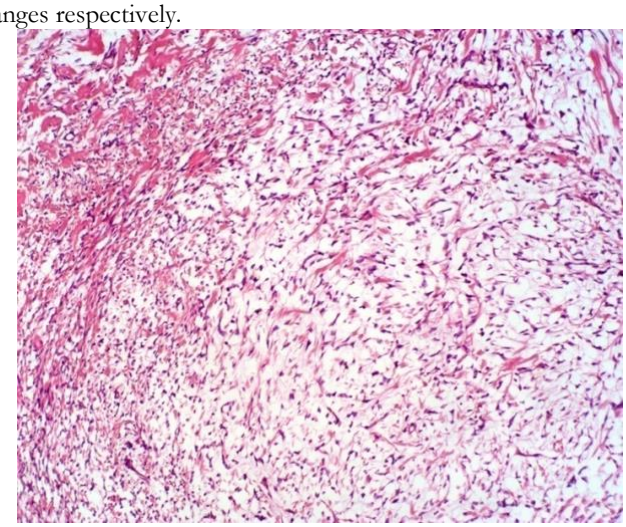

Figure 3: Photomicrograph showing histoarchitecture of myxoid leiomyoma. Note the spindled cells with bland nuclear features and connective tissue with myxoid areas. H and E x400.

Discussion

Grossly, leiomyomas are typically multiple or solitary, spherical, and firm while the cut surface is white to tan and has a whorled trabecular texture. In our study, solitary nodule was observed in 56(29.2%) cases while multiple nodules were found in the remaining 136(70.8%) cases. Our findings were similar to results obtained by Abraham and Saldanha who observed solitary leiomyoma in 42.5% of cases and multiple leiomyomas in 57.5%.[4] Similarly, Sarfraz et al also observed multiple nodules in 60.87% of cases studied.[5] Our findings were however discordant with other studies.[6-9] Ukwenya et al also showed that 40.9% and 59.09% of cases of leiomyoma diagnosed were multiple and solitary leiomyomas respectively.[6] Similarly, a study

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conducted in Saudi Arabia showed that 47.9% and 52.1% of cases of leiomyoma were multiple and solitary respectively.[7] A study in the European nation of Slovenia showed the presence of solitary and multiple leiomyomas in 57.9% and 42.1% of cases studied respectively.[8] Lahori et al also 56.96% of leiomyomas were single and 43.04% were multiple.[9] Discrepancy may be due to diagnostic methods or geographical locations. Sub-serosal, submucosal, and small-sized fibroids are sometimes misdiagnosed or missed during routine ultrasonography. However, careful examination of hysterectomy specimens in pathology laboratories would often reveal nodules that were not detected during clinical imaging.[1,10]

Uterine leiomyomas are classified according to their location into intramural, submucosal, and sub-serosal types. The majority of the leiomyomas in our study were intramural 176(91.7.%) followed by submucosal 25(13.0%) and submersal 23(12.0%). These findings were similar to a study by Goyal et al that reported that most of the leiomyomas were intramural 100(66.6%) followed by subserosal23(15.3%) and submucosal 09(6.0%).[11] Gowri et al and Abraham J et al reported similar findings.[4,12] Uterine leiomyomas can be found in more than one location in the same hysterectomy specimen. In this study, 26(13.5%) patients had nodules in more than one location with intramural and submucosal nodules accounted for 12(6.3%). Similar findings were reported by Goyal et al.[11] There was a significant statistical association between the age group of patients with leiomyoma and submucosal nodules with a p-value of 0.008. None of the patients in the third decade presented with submucosal nodules. A review of the literature shows sub-mucosal nodule is usually associated with menorrhagia or abnormal uterine bleeding and most patients present with leiomyoma while seeking treatment for infertility treatment.[6] Also, leiomyoma starts within the myometrium before migrating to other locations in the uterus.[6]

Histological variants of leiomyomas have been described in the literature.[2,4,9] Histologically, leiomyoma is usually composed of interlacing fascicles of smooth muscle cells with cigar-shaped nuclei and elongated cytoplasm. The vast majority of cases were of the usual or conventional type as seen in this study and it accounted for a total of 182(94.8%) cases. This shows that usual was the commonest in our environment which was lower than findings from work done by Lahori et al which showed that the usual type of leiomyoma accounted for 53.2% of cases.[9] Similarly, the findings from our present study also agree with those from a study by Manjula et al, who reported that 95.5% of leiomyomas were of the usual histology type.[13]

Cellular leiomyoma accounted for less than 1% of leiomyomas in this study. This was in contrast to a study by Lahori et al which who reported 5%.[9] By definition, cellular leiomyoma shows cellularity that is greater than that of the surrounding myometrium. The isolated occurrence of hypercellularity may suggest a diagnosis of leiomyosarcoma, but cellular leiomyomas lack tumour cell necrosis and moderate to severe atypia and have infrequent mitotic figures. A cellular leiomyoma comprised of small cells with scanty cytoplasm can be confused with an endometrial stromal tumour.[2]

Out of 192 cases under review, there was only 1 case (0.5%) of epithelioid leiomyoma. Manjula et al also reported that epithelioid leiomyoma accounted for 0.22% of leiomyomas studied and that they are composed of epithelial-like cells.[13] They are rare and the criteria predictive of their malignant behaviour are less well established than that for spindle-cell smooth muscle tumours.[2,13] Small size, circumscribed margin, presence of clear cytoplasm, extensive hyalinization, and lack of necrosis are parameters associated with a favourable prognosis whereas those with two or more of the following criteria including size larger than 6 cm, 2-4 mitotic figures/10 HPFs, moderate to severe atypia and necrosis, should be classified as those with epitheliod tumour of uncertain malignant potential.[2]

Myxoid leiomyoma accounted for 1% of the cases studied. Manjula et al reported similar findings.[13] Myxoid leiomyoma is composed of benign smooth muscle cells with myxoid material separating the tumour cells. The margins are circumscribed and neither cytological atypia nor mitotic figures are present.[2]

Lipoleiomyomas accounted for 1.6% of cases reviewed in this study. Literature review showed that it accounted for 0.03% to 0.2% of leiomyoma. Histologically, it is characterized by admixture of varying amounts of mature adipose tissue with smooth muscle cells.[2]

Besides the usual variant which is very common, other histological types of leiomyomas are rare,

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however, it is important to recognize them because some of them are great mimics of malignancy, constituting an important source of diagnostic errors.[14]

Furthermore, the appearance of a leiomyoma often is altered by degenerative changes.[14] Degenerative changes seen in leiomyomas include hyalinization, cystic change, red degeneration, and calcification. In this study, degenerative changes were seen in 124 (64.6%) of leiomyomas. Hyaline change was the commonest degenerative change seen occurring in 115 cases (59.9%), followed by cystic change which was identified in 20 cases (10.4%) while red degeneration was the least frequent change which was seen in only 3 cases (1.6%). This finding is corroborated by a similar study in Zaria, Nigeria where degenerative changes were seen in 73.2% of cases with hyaline degeneration being the commonest, accounting for 57.9% of the cases.[15] Goyal et al also reported also reported that 56.8% of leiomyomas had hyaline change. Similar findings were reported in studies by Begum et al and Dayal et al.[16,17]

The degenerative or secondary changes in leiomyomas occur due to inadequate blood supply. The type of secondary changes depends on the rapidity and degree of vascular insufficiency. In red degeneration, tumour overgrows its blood supply leading to necrosis and haemorrhage. In this study, there was a significant association between red degeneration and age group of patients with leiomyoma. In our study, all (1.6%) cases of red degeneration reported were seen in third decades. Red degeneration in leiomyoma is reported more often during pregnancy due to rapid growth of the tumour. It is also reported during the postpartum period and in women taking oral contraceptives.[18,19]

Strengths and limitations of the study

Our strengths lie in the comprehensive of data extracted and analyzed for this study. Also, this topic is understudied in the country. This study is also limited by possibility of selection bias because it was conducted at a tertiary health centre and retrospective in nature which implies that the results obtained may not be applicable to the general population.

Conclusion

Leiomyoma is a benign tumour of uterine smooth muscle which is commonly seen in reproductive age women. Most of the women with uterine leiomyoma presented with multiple nodules. An intramural site was the most common location, hyaline change was the most common degeneration and usual variant was the most common subtype seen in our study. Also, the pathologist needs to be cautious while diagnosing rare histological variants of leiomyoma as they could mimic malignant transformation.

Declarations

Ethical Consideration: Permission for the conduct of this study was obtained from the Ethical Review Committee of the LTH, Ogbomoso. This study was also performed in compliance with the guidelines of the Helsinki Declaration on biomedical research on human subjects.

Authors' Contribution: AAA contributed to the designing, analyzing and writing up the manuscript. He also reviewed all the slides and collated the data. SD reviewed the slides and manuscript. AEOA reviewed the slides and manuscripts. AO, RMW, and INA reviewed the manuscript.

Conflict of interest: Authors declare no conflicts of interest.

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